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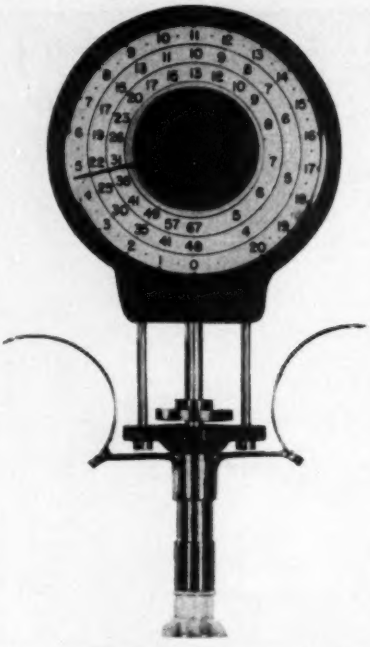

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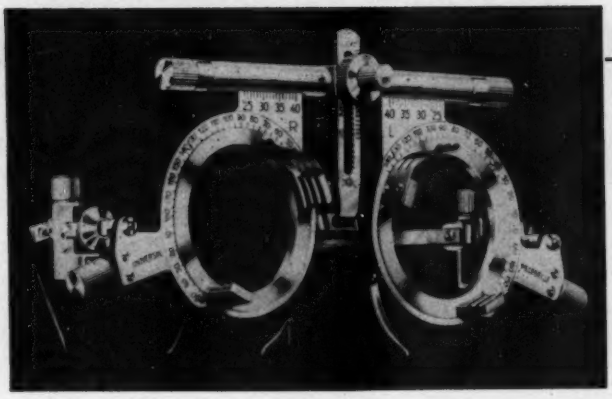

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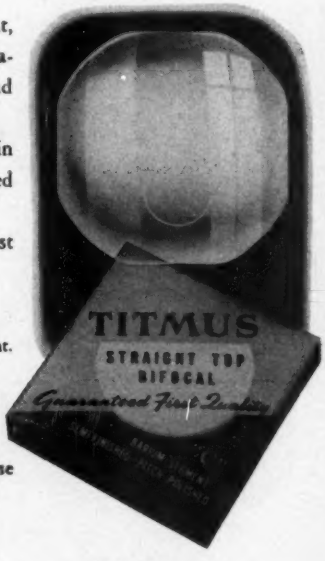

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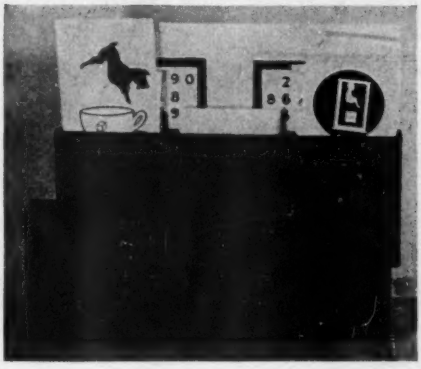

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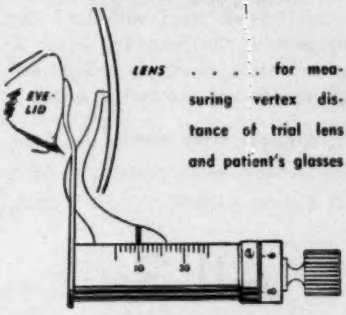

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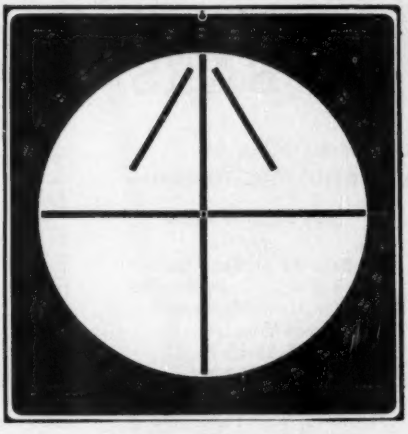

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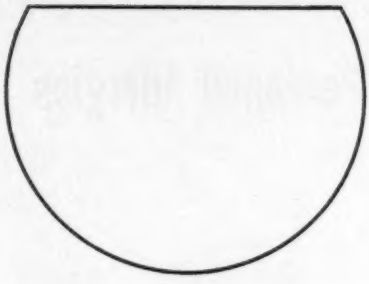

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SURGERY OF THE LENS IN INFANCY AND CHILDHOOD

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I AM HONORED to be invited to give the first John E. Weeks Memorial Lecture. Dr. Weeks was interested in all aspects of ophthalmology, and especially in ocular surgery, and would therefore have been interested in my subject. The procedures I shall advocate are based partly on theoretical considerations, partly on the experience of others but chiefly on my own experience.

Disorders of the lens which may require surgical treatment in infancy and childhood include (1) congenital cataract, (2) traumatic cataract, (3) cataract associated with uveitis and (4) congenital dislocation of the lens and microphakia or spherophakia.

CONGENITAL CATARACT

There are many types of congenital cataract, ranging from bilateral complete cataract to insignificant congenital opacities, requiring no treatment. In general, the type of cataract has little to do with the indication for operation, though it may influence the choice of operation. From a surgical standpoint, congenital cataracts may be classified as follows:

1. Bilateral complete cataract, either present at birth or developing during the first few months of life.
2. Severe involvement of both eyes without complete opacification of the lenses, as in large and very dense zonular cataracts.
3. Mild involvement of the lens of one eye and severe involvement of the other.
4. Bilateral dense central opacities, allowing adequate vision with dilated pupils but permitting inadequate vision when the pupils are small.
5. Moderate involvement of both eyes.

In the first group, that of bilateral complete cataract, there can be no question that operation in indicated. The same is true of the second group when the opacity is obviously of sufficient size and density as to preclude useful vision. In the third group, in which the involvement of one eye is of mild degree, the question may be discussed whether operation is justified on the worse eye. If the vision in the better eye is 20/50 or higher under all conditions, that is, whether the pupil is large or small, the patient will be able to lead a fairly normal life so far as the visual handicap is concerned if no operation is done. To be sure, if the involvement of the lens of the poorer eye is very severe, the eye may become amblyopic, but this is not invariably true. On the other hand, if operation is done on one eye, that eye is certain to become amblyopic. Theoretically such postoperative amblyopia could be prevented by prescribing a cataract lens and occluding the good eye.

From a practical standpoint this method does not work out very satisfactorily. It is difficult in many cases to make an accurate refraction; it is much harder to secure satisfactory cooperation on the part of parents and child than in cases of squint, and in most instances occlusion is given up sooner or later, without its having accomplished its purpose. Considering this fact, as well as the hazards and complications of surgical therapy, it is my opinion that in these cases operation should not be done.

In the fourth group, satisfactory vision may be obtained by keeping the pupils dilated and prescribing suitable lenses. This is usually not feasible over a long period of years, and operation needs to be done. If vision is of the order of 20/40 to 20/50 even with small pupils, probably no operation should be done.

In the fifth group, with moderate involvement of both eyes, will be found many borderline cases so far as the question of operation is concerned. If vision is 20/50 or better under all conditions, I believe that no operation should be performed. If vision is 20/70, probably operation should be done in most cases, but at this level of vision the decision will depend somewhat on how the child gets along in school. Furthermore, one must decide whether or not in a given case the opacity of the lens accounts for the loss of vision. Vision of 20/70 or less is not an indication for operation if the lenticular opacity does not account for the poor vision. In any borderline case it is important not to hurry into operation early in the child's life. Amblyopia does not develop in these cases, and one should wait until the child is 5, 6 or 7 years of age, so that an accurate refraction can be done and one can be absolutely sure that corrected vision is below the critical level.

Operations commonly employed for congenital cataract are (1) simple discission, (2) through and through discission, (3) discission followed by linear extraction or removal of lens matter by suction through a small incision, (4) linear extraction alone, (5) linear extraction with iridectomy and (6) optical iridectomy. Each procedure has its advocates, and many series of cases have been reported in which these various technics have been employed. With each of the procedures a good percentage of favorable results has been obtained, but some unfavorable results with various complications have been encountered with all the technics. The chief complications of operations for congenital cataract are glaucoma, an inadequate pupillary opening and detachment of the retina. Less common complications are uveitis, epithelization of the anterior chamber and corneal edema with bullous keratitis.

What are the causes of these complications, and what methods may be employed in avoiding them?

Glaucoma.—How does glaucoma come about in operations for congenital cataract? Though the mechanism of production of the glaucoma is far from clear in all cases, certain obvious causes may be discussed.

1. Rapid swelling of the lens after discission, pushing the iris forward and blocking the angle. This complication occurs when the opening in the capsule is too small and the lens swells as a whole. It can be avoided by making a wide opening in the capsule from top to bottom and from side to side, as advocated by Greenwood.[1] If this is done, the lens cannot swell as a whole and block the angle.

1. In discussion on Wilder, W. H.: Operative Procedures and Method of Handling Juvenile Cataract, Tr. Am. Acad. Ophth. **33**:113-131, 1928.

As the lens takes up fluid and tends to swell, cortex is extruded into the anterior chamber, and glaucoma from swelling of the lens is prevented.

2. A large amount of cortex in the anterior chamber, presumably blocking the angle. Actually, glaucoma from this cause rarely occurs to a degree requiring further surgical intervention. A moderate elevation of tension is well tolerated by the eye and usually subsides spontaneously.

If severe glaucoma results from rapid swelling of the lens as a whole or from excess cortex in the anterior chamber, it can be promptly relieved by linear extraction.

3. Block of the pupil by a membrane, with iris bombé. This complication may occur if the pupil is not well dilated and if there is considerable postoperative inflammation—iritis or uveitis—which adds an inflammatory membrane to the capsular remnants and completely seals off the pupillary opening. If iris bombé with glaucoma ensues, and it has not been present too long, it can be completely relieved by transfixion of the iris or by iridectomy. Glaucoma from this cause may largely be avoided if it is possible to get and to maintain an adequate dilation of the pupil. If the pupil has become small and cannot be dilated and a pupillary membrane is present, iris bombé can be prevented by a prophylactic transfixion of the iris or by iridectomy.

4. Delayed reformation of the anterior chamber after discission or linear extraction, leading to the formation of peripheral anterior synechias. After discission there is never delay in reformation of the anterior chamber if the puncture is made in a slanting fashion, so that after the knife is withdrawn the incision closes like a valve. In the case of linear extraction, if the incision is corneal, it should also be beveled, as advocated by Barkan [2] and Cordes,[3] and it likewise closes like a valve. If the incision is made behind the limbus, an adequate suture should be employed to insure a tight closure of the wound. Whatever type of operation is employed, air should be injected to form the anterior chamber at the conclusion of the operation. Every attempt should be made to prevent incarceration of iris or lens material in the wound—both of which are frequent causes of peripheral anterior synechias and glaucoma.

5. Block of the pupil by vitreous and filling of the anterior chamber with vitreous. This mechanism of glaucoma following surgical measures for congenital cataract may often be overlooked because it may not be suspected, and because of the difficulty of slit lamp examination in a young child. It may occur after linear extraction but is most commonly seen after repeated discissions. With discission, a *sine qua non* for this complication is a small pupil, or a pupil of any size if it is completely blocked by a membrane. Then when one cuts into the vitreous, it may come forward and produce a block of the pupil. As pressure builds up in the posterior chamber, an iris bombé may first be produced; later, vitreous may be forced into the anterior chamber, even completely filling it. It is probable that this mechanism is the chief cause of the gross peripheral anterior synechias not infre-

2. Barkan, O.: A Procedure for the Extraction of Congenital, Soft, and Membranous Cataracts, Am. J. Ophth. **15**:117, 1932; Operation for Congenital Cataract, Arch. Ophth. **40**: 680 (Dec.) 1948.

3. Cordes, F. C.: Surgery of Congenital Cataracts, Am. J. Ophth. **31**:1073, 1948.

quently seen in patients who have had multiple discissions for congenital cataract. Once glaucoma has been produced by this mechanism and the anterior chamber is filled with vitreous, the indications for treatment are transfixion of the iris in the periphery or iridectomy. Transfixion involves less risk to the eye and is usually adequate. Iridectomy is to be preferred if vitreous is in contact with the cornea and causing edema or bullous keratitis. In such a case some loss of vitreous is necessary if the cornea is to be saved. Results of treatment are far from satisfactory, and the eye may be lost. Every possible safeguard, therefore, should be employed for prevention of this complication, since treatment is not always effective. Filling of the anterior chamber with vitreous after linear extraction can largely be avoided if certain points in technic are observed; these will be discussed later. The complication occurs most commonly after discission and can be avoided in nearly all cases if certain rules are observed. First, one should disturb the vitreous as little as possible with the discission needle. Second, and this is the most important point of all, one should adhere without exception to von Graefe's dictum, "Never do a needling in the presence of a small pupil." If a pupillary membrane is present which requires discission and the pupil is small and undilatable, one must, either before or at the time of the needling, perform an iridectomy or a peripheral transfixion of the iris. The latter is a simpler procedure and is usually adequate. It is my opinion that the mechanism of pupillary block by vitreous and filling of the anterior chamber with vitreous is the principal cause of disastrous glaucoma following operation for congenital cataract and that it is largely preventable if proper prophylactic measures are employed.

Inadequate Pupillary Opening.—The surgeon may sometimes fail to secure an adequate pupillary opening, even after repeated operations. This failure may be due to the formation of a dense membrane, partly inflammatory, and difficult to divide with a discission needle. In such cases, if a good opening cannot be secured by needling, rather than keep repeating the procedure, one is probably wiser to divide the membrane with Noyes scissors, taking due precautions against subsequent pupillary block by vitreous. A slanting incision is made with a keratome; a small peripheral iridectomy is done; the iris is punctured with a sharp narrow knife halfway between the limbus and the pupillary border, the posterior blade of the scissors being permitted to pass behind the iris and membrane, and a cut or cuts are made through the iris and the pupillary membrane. Iridotomy is usually preferable to discission in all cases in which the pupil is very small. It is difficult to secure a satisfactory opening in these cases by discission; and even if a tiny clear opening is secured, it tends to close later, either from proliferation of the capsule or from the development of an inflammatory membrane.

Detachment of the Retina.—Late detachment of the retina is not infrequent after operations for congenital cataract. Not many statistics are available [4]; but, such as they are, they indicate that detachment may occur many years after opera-

4. Shapland, D. C.: Retinal Detachment in Aphakia, Tr. Ophth. Soc. U. Kingdom **54**: 176, 1934; Bilateral Aphakic Retinal Detachment, Proc. Roy. Soc. Med. **39**:834, 1946. Knapp, A.: Operative Prognosis of Congenital Cataract, Arch. Ophth. **32**:519 (Dec.) 1944. Moore, F., in discussion on Greeves, R. A.: Diathermy in Ophthalmology, Tr. Ophth. Soc. U. Kingdom **53**:487, 1933.

tion. When it does occur in these cases, the prognosis is very poor for successful attachment by operation. It is important, therefore, to employ all possible measures to avoid this complication. Unfortunately, the factors which produce detachment are not as yet clearly understood, and its avoidance is not always possible.

The first point to be considered in avoiding detachment of the retina in these cases of congenital cataract is not to operate on the patient in the first place. It is with detachment of the retina, as well as other complications, in mind that one decides against operative intervention in a patient with the handicap of 20/50 vision, but one who can, nevertheless, carry on a fairly normal life without operation. If operation is done, it is probable that the more the vitreous is disturbed, as with repeated operations, especially if vitreous is allowed to come forward into the anterior chamber, the greater the danger of late detachment of the retina.

The goal of congenital cataract surgery is an adequate pupillary opening and the avoidance of complications. If this goal is attained, the operative procedure must be considered completely successful, even though central vision may not be particularly good, owing to amblyopia or other causes. By what method is this goal best achieved?

Simple Discission of the Lens.—This procedure is probably employed by more ophthalmologists than any other method. Results reported by many authors are generally good.[5] It is certainly not the best operation if the pupil cannot be easily and fully dilated with atropine or scopolamine before operation. If the pupil cannot be well dilated prior to operation without the additional use of epinephrine or phenylephrine U. S. P., it is certain that it will be less well dilated after operation. In such cases, almost invariably posterior synechias develop, and one may encounter all the complications listed above which are directly attributable to the small pupil.

Through and Through Discission of the Lens.—This operation has been advocated by several ophthalmologists.[6] It is said to have the advantage that one operation is usually sufficient. A theoretical disadvantage is that it entails more disturbance of the vitreous, with its possible late consequences. A real disadvantage is that if glaucoma should follow such operation and a linear extraction were attempted to relieve the glaucoma, the danger of loss of vitreous, with its attendant complications, would be very great. This operation is still preferred by some ophthalmologists but has never become as popular as simple discission or linear extraction. I have had no personal experience with this operation. To me, its disadvantages seem to outweigh its advantages.

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5. (*a*) Wilder, W. H.: The Operative Procedures and Method of Handling Juvenile Cataract, Tr. Am. Acad. Ophth. **33**:113, 1928. (*b*) Klare, D.: Klinische Erfahrungen bei der operativen Behandlung des grauen Stares im Kindesalter, Arch. f. Augenh. **102**:230, 1929. (*c*) Owens, W. C., and Hughes, W. F., Jr.: Results of Surgical Treatment of Congenital Cataract, Tr. Sect. Ophth., A. M. A., 1947, p. 229. (*d*) Falls, H. F.: Developmental Cataracts: Results of Surgical Treatment in 131 Cases, Arch. Ophth. **29**:210 (Feb.) 1943.

6. Ziegler, S. H.: Complete Discission of the Lens by the V-Shaped Method, J. A. M. A. **77**:1100 (Oct. 1) 1921. Goar, E. L., and Potts, C. R.: Relationship of Rubella in the Mother to Congenital Cataracts in the Child, Am. J. Ophth. **29**:566, 1946. Berens, C.[1] Weiner, M.[1] Benedict, W., in discussion on Dean, F. W.: Cataracts: Operation for Congenital and Juvenile, Tr. Am. Acad. Ophth. **31**:261, 1926. Bell, G. H.: Operation for Juvenile Cataract in Two Stages, Am. J. Ophth. **9**:433, 1926.

Linear Extraction.—This operation has been used for many years and has been recommended in recent years particularly by Barkan, Cordes, Bagley and others.[7] It has the advantage of getting rid of the lens quickly, and if properly performed it appears to be followed by fewer complications than is discission. Linear extraction of the lens is, however, in no sense a minor operation, and serious complications can occur. Owens and Hughes [5c] reported a 16.1 per cent, and Bagley [7d] a 10 per cent, loss of vitreous. Loss of vitreous in these cases must be regarded as a catastrophe, for it not infrequently results in ultimate loss of the eye.

The following technic has proved most satisfactory in my hands.

The incision is best made with a keratome, for it can thus be beveled to a greater degree and more satisfactory closure can be obtained. A corneal incision is preferred by some surgeons [8] and is undoubtedly less traumatic. With this incision, however, it is more difficult to do a peripheral iridectomy. For this reason, I prefer a limbal incision under a conjunctival flap with suture of the wound. An incision 5 to 6 mm. in width is sufficient in most cases. Occasionally a nucleus will be encountered which is too large to be delivered through such a wound, and the incision must be enlarged with scissors. The anterior capsule is torn off with toothed capsule forceps. Whether or not a good piece of capsule is obtained with this first bite, the forceps should not again be introduced into the anterior chamber in an attempt to remove another piece of anterior capsule. It must be remembered that in these young patients there is often little, if any, nucleus present. When the anterior capsule is once opened, cortex spills forward, and the posterior capsule may advance to a position near that formerly occupied by the anterior capsule. A second attempt with forceps may therefore, instead of removing another piece of anterior capsule, actually remove a piece of the forward displaced posterior capsule, and the surgeon is dismayed to encounter loss of vitreous early in the operative procedure. After the capsule is opened, a spoon held in the left hand is introduced into the anterior chamber as far as the upper pupillary border, and the iris is gently depressed. Cortex is then milked out by gently stroking the cornea with another instrument, held in the right hand. One should not apply pressure, as in a regular cataract extraction. During this maneuver the operator must be constantly aware of the position of the spoon with which the iris is depressed above. Unless he makes a point of it, he may forget what the left hand is doing and inadvertently push the spoon back into the vitreous. When no more cortex can be milked out, the spoon is withdrawn from the anterior chamber, which is then irrigated with saline solution. Whatever cortex and capsule it is possible to remove by irrigation usually comes out quickly, and prolonged irrigation accomplishes nothing further and may result in loss of vitreous. When no more material can be removed by irrigation, the operation should be terminated. It is inadvisable at this point ever to introduce forceps in an attempt to remove a last bit of cortex or capsule. The hazards of such a maneuver far outweigh any possible gain. The mark of the skilful linear extraction surgeon is said to be the ability to know when to quit.

It is my opinion that iridectomy should be a part of every linear cataract extraction. The iridectomy may be peripheral if the pupil dilates well with atropine or scopolamine; it should be full if the pupil does not dilate well or if the iris shows a strong tendency to prolapse. Iridectomy lessens the danger of postoperative prolapse of the iris and is good insurance against the possibility of a blocked pupil at some later date. The anterior chamber should always be reformed with an injection of air at the conclusion of the operation.

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7. (*a*) Barkan.[2] (*b*) Cordes.[3] (*c*) Owens and Hughes.[5c] (*d*) Bagley, C. H.: Congenital Cataracts: Survey of Various Types of Operation, Am. J. Ophth. **32**:411, 1949. (*e*) Chechik-Kunina, E. A.: Comparative Evaluation of Surgical Procedures for Removal of Soft Cataract. Publications Helmholtz Institute of Ophthalmology (Russia), 1940, p. 553; abstracted, Am. J. Ophth. **25**:1392, 1942. (*f*) Alexander, G. F.: The Immediate Removal of Congenital Cataracts, Tr. Ophth. Soc. U. Kingdom **48**:94, 1928.

8. Barkan.[2] Cordes.[3]

Discission followed by linear extraction has been advocated.[9] This method adds a general anethesia with its attendant risks; otherwise, the results and complications are comparable to those in linear extraction alone, with the advantage of more complete removal of the lens cortex. If linear extraction is done after preliminary discission, one should not attempt to remove pieces of the anterior capsule with forceps either before or after the cortex is evacuated. As stated above, this involves the risk of injury to the posterior capsule and subsequent loss of vitreous. Dean[10] and Wolfe[11] stated that they prefer sucking out the cortical material through a small corneal incision.

Linear Extraction with Complete Iridectomy.—This operation has been employed in a large series of cases by Horay[12] with very favorable results.

Optical Iridectomy.—This operation has been advocated for certain patients whose opacity is central and in whom vision of 20/40 to 20/50 is possible with a dilated pupil but is considerably less when the pupil is small.[5b] Such patients are particularly handicapped when out in bright light and when reading. It would appear that optical iridectomy is a logical choice for such patients. The operative complications are infinitely less than with any operation designed to get rid of the lens. Some ophthalmologists have advised against this procedure without offering any very convincing reasons for this opinion.[13] I have had a single experience, with a very favorable result. The iridectomy is usually done in the lower nasal quadrant.

Comment.—Which of these operations is to be recommended in the treatment of congenital cataract? Judging from the reports in the literature and from my own experience, it would appear that no one operation is to be recommended to the exclusion of all others. The type of eye to be operated on should determine the choice of operation in each case.

In the case of simple zonular cataract, if a full dilation of the pupil can be obtained preoperatively with atropine alone, one may employ simple discission, discission followed by linear extraction or simple linear extraction with almost equally good results, though some reports record better results and fewer complications with linear extraction.[14] Of course, a much longer time must elapse before all cortex is absorbed with discission alone than with linear extraction with or without preliminary discission, and during this longer convalescent period there is greater danger of the pupil's becoming small and more or less bound down. On the other hand, linear extraction, unless performed with judgment and skill, may involve more serious operative complications, such as prolapse of the iris and loss of vitreous.

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9. Klare.[5b] Falls.[5d] Krückmann, E.: Über eine Methode zur Entfernung des Schichtstares, Arch. f. Ophth. **90**:322, 1915.

10. Dean, F. W.: Cataracts: Operation for Congenital and Juvenile, Tr. Am. Acad. Ophth. **31**:261, 1926.

11. Wolfe, O. R., and Wolfe, R. M.: Removal of Soft Cataract by Suction: New Double-Barreled Aspirating Needle, Arch. Ophth. **26**:127 (July) 1941.

12. Horay, G.: Über Staroperationen im Kindesalter, Klin. Monatsbl. f. Augenh. **71**:178, 1925.

13. Moncreiff, W. F.: Contributions to the Surgery of Congenital Cataract: Modification of Discission in Preschool Age Group, Am. J. Ophth. **29**:1315, 1946.

14. Klare.[5b] Owens and Hughes.[5c] Falls.[5d] Bagley.[7d]

In the case of bilateral complete cataract in infancy complete iridectomy with linear extraction is, I believe, the operation of choice. It is often impossible in such a case to get a good dilation of the pupil before operation, and if discission or simple linear extraction is done, the pupil very often becomes small after operation and more or less bound down, with all the evil consequences of this condition. Furthermore, it is often difficult to divide with a needle the lens plaque often encountered in these cases. Iridectomy widens the pupil and prevents the consequence of the small pupil. One operation usually suffices, though a secondary discission is sometimes necessary. Linear extraction is the operation of choice in cases of the dense central "collar button" type of opacity, which is very difficult to divide with a needle. Complete iridectomy with linear extraction is, I believe, to be preferred in all cases in which it is not possible to get a good dilation of the pupil prior to operation. In so-called membranous cataract, the lens may have beeen entirely absorbed except for the capsule, or there may be a small amount of cortical material between two layers of capsule. Discission usually gives a good result in cases of this type, but if the membrane cannot be divided with a discission needle, it can be cut with Noyes scissors. I believe it is never advisable to pull out a pupillary membrane with forceps.

What is the optimum age at which to operate for congenital cataract? Judging from reports in the literature, this point is still a very controversial one. In the case of zonular cataract, in which amblyopia does not ordinarily develop, it is probably wise, except with obviously very severe involvement of the lens, to defer operation until the child is 6 or 7 years of age, so that one can be absolutely sure what the best corrected vision is. If one hurries into operation on these children at an early age, one may sometimes operate unnecessarily.

In the case of bilateral complete, or nearly complete, cataract in infancy, there is the greatest difference of opinion as to the optimum time for operation. On the one hand are those [15] who advocate early operation to permit development of the macula, and on the other hand are reports [16] indicating that the results are definitely poorer when operation is done before the age of 2 years than when it is done later.

No convincing statistics are available indicating better development of the macula and ultimate better vision when operation is done early. Nevertheless, the assumption is a reasonable one, and there can be no doubt that the child develops faster as a whole if given vision as early as possible. One must face the fact, however, that in many of the reported series the ultimate visual results are poorer and the incidence of complications apparently greater if operation is done when the child is under 2 years of age.[16]

The reports of unfavorable visual results may be misleading, for in cases of bilateral complete cataract nystagmus is often present and, even if a good pupillary opening is secured and there are no operative or postoperative complications, the visual results are not comparable to those usually obtained in cases of zonular cata-

15. Klare.[5b] Horay.[12] Elschnig, A.: Augenärtzliche Operationslehre, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1922, p. 1191. Meller, J.: Augenärtzliche Eingriffe: Ein kurzes Handbuch für angehende Augenärzte, ed. 4, Vienna, Springer-Verlag, 1938, p. 252.

16. Owens and Hughes.[5e] Falls.[5d] Bagley.[7d] Kiss, W.: Sehschärfe der in früher Kindheit doppelseitig Staroperierten, Klin. Monatsbl. f. Augenh. **98**:523, 1937.

ract. The greater actual incidence of complications, however, cannot be dismissed lightly. To what cause can these complications be attributed, and how can they be avoided, so as to make operation on the youngest patient as safe as on the older? A clue may be found in the report of Horay.[12] In his series the results in patients operated on under 1 year of age were as good as when operation was done later. The operation he employed was iridectomy and linear extraction. With this method he avoided the small, bound-down pupil after operation, which, as stated above, is probably the chief cause of complications in these cases. If this operation is employed, and proper small instruments are used, I believe there is no reason that operation cannot be done when the patient is under 1 year of age, with the possibility, at least, of the child's ultimately acquiring better vision than if operation were done later. After all types of operation for congenital cataract, one cannot overemphasize the importance of the long-continued postoperative use of atropine or scopolamine. If use of the mydriatic is discontinued before all cortex is absorbed, posterior synechias may develop.

TRAUMATIC CATARACT

Traumatic cataract may be produced in childhood by severe contusion of the globe, but in the great majority of instances it is the result of a perforating wound of the anterior segment. There may be perforation of the anterior capsule only, and the size of the opening in the capsule largely determines the rate of development of the cataract. In other cases there is through and through perforation of the lens, as with a narrow-pointed instrument or by an intraocular foreign body.

In traumatic cataract, glaucoma may result from swelling of the lens if the perforation in the anterior capsule is small. If the glaucoma is severe, it is treated by prompt linear extraction. If the perforation is large, cortex tends to extrude into the anterior chamber as the lens swells, and glaucoma is less frequently encountered.

In the treatment of traumatic cataract in childhood, it must be remembered that unless severe glaucoma develops one need be in no hurry in one's surgical treatment if, as is often the case, the fellow eye is good. In a large number of cases, particularly if there is a large opening in the anterior capsule, the lens will completely absorb in two or three months without any operative intervention. If, however, no evidence of absorption of the lens can be observed over a period of time, operative measures may be undertaken. If there are definite indications that the anterior capsule only has been perforated, either discission or linear extraction is permissible. If there is doubt as to whether the perforating agent has gone through the lens, or there is clear evidence that it has done so, linear extraction is to be avoided if possible. If the posterior capsule has been perforated, the hyaloid membrane has likewise been injured, and loss of vitreous is a not uncommon complication of linear extraction in this case. In such a condition discission of the lens is much to be preferred.

In the case of cataract due to severe contusion one has every reason to infer that a force sufficient to cause a cataract may well have ruptured the hyaloid membrane. In the case of contusion cataract, therefore, linear extraction may be a hazardous procedure, and the eye is best treated by discission. In cataract due to contusion there may be some degree of dislocation of the lens. In this condition discission is

likewise the safest procedure. If the zonule is extensively torn, it may be advisable to use two needles, fixating the lens with one while the discission is performed with the other.

In the case of unilateral traumatic cataract, when the lens has been gotten rid of either by spontaneous absorption or by operation, there often remains a pupillary membrane. Should a final discission be made to secure a good pupillary opening in such a case? Since the eye will not be used, there would seem to be unnecessary risk in such operation. I believe that operation should be deferred until such time as the eye is needed for vision, unless the surgeon intends to carry out occlusion to prevent amblyopia.

The points concerning dilation of the pupil, the dangers of a small pupil and pupillary block, discussed in connection with congenital cataract, are equally pertinent in the treatment of traumatic cataract.

CATARACT ASSOCIATED WITH UVEITIS

One sometimes encounters severe intractable bilateral uveitis in children. In some cases it is a part of Still's disease (multiple rheumatoid arthritis), but in others no abnormality can be found aside from the uveitis. Treatment of the uveitis is often ineffective, and finally the vision is reduced to a very low level, owing to opacification of the lens or to the development of a dense pupillary membrane. Band keratitis is a common complication. Oven a period of years the inflammation usually subsides completely or becomes of very low grade, with the only evidence of possible activity a slight aqueous flare. Sooner or later one must face the prospect of removal of the lens as offering the only possibility of restoration of vision. Before undertaking lens extraction, one would prefer the uveitis to have been quiescent for a considerable period. There are cases, however, in which a mild aqueous flare never disappears, and if one defers operation until it is gone the child may become an adult before the operation is performed. One should not, therefore, wait indefinitely before attempting to restore vision.

What operation should be performed? It is common experience that extracapsular cataract extraction in cases of severe long-standing plastic uveitis in the adult may be followed by loss of the eye. This is no less true in childhood. If linear extraction is performed in these cases, the result will often be atrophy of the globe. The operation to be preferred in all cases, regardless of age, is intracapsular extraction. A full cataract section is made. Corneoscleral sutures are used, as in the adult. An iridectomy is done, and the iris is carefully separated from the lens with a spatula. This may be a difficult procedure and require a great deal of time and patience. The next step is inferior iridotomy.[17] The iris is split as far as possible toward the 6 o'clock position with Noyes scissors. When this is done, there is better dilation of the pupil after operation, and the possibility of a drawn-up pupil is usually obviated. An attempt is then made to remove the lens in the capsule by whatever method is most successfully employed by the surgeon. One finds that it is usually not more difficult to dislocate the lens in such a child's eye than in the senile eye. Most of these eyes survive the operation well, and useful vision is obtained, even though mild evidences of uveitis continue indefinitely.

17. Chandler, P. A.: The Value of Inferior Iridotomy in Operations for Cataract on Eyes with Posterior Synechiae or Pupillary Membrane, Tr. Am. Ophth. Soc. **36**:171, 1938.

CONGENITAL DISLOCATION OF THE LENS

Congenital dislocation of the lens may be associated with other abnormalities, such as those in Marfan's syndrome (arachnodactyly). The lens may be dislocated in any direction. The dislocation may be very slight, so that vision is entirely through the lens, or it may be more marked, so that both phakic and aphakic vision may be possible. In other cases the lens may be completely dislocated backward into the posterior chamber. The lens may also come into the anterior chamber. The surgical implications of congenital dislocation of the lens depend on the degree and direction of dislocation and on the corrected vision of the eye.

All congenitally dislocated lenses are small and more spherical than the normal lens and produce a considerable degree of myopia, usually 10 to 15 D. or more. Various degrees of dislocation may be considered.

The dislocation may be slight, with vision entirely through the lens. A considerable degree of lenticular myopia is always present. Accurate refraction is difficult, since retinoscopy is unsatisfactory. Some of the affected children are severely handicapped visually, but it is seldom possible to make an accurate evaluation of the visual status until a child is 5 or 6 years of age. The question of operation should, therefore, be deferred until one can be reasonably sure of the level of corrected vision. Though distance vision may be poor, many of these children are able, owing to the myopia, to read the finest print close to the face. If the vision is 20/70 or less, operation must be seriously considered. If operation is decided on, what is the procedure of choice?

Intracapsular extraction of the lens has been employed, and successful results have been reported.[18] Since loss of vitreous is a frequent accompaniment of such extraction, various complications may ensue. The greatest to be feared is detachment of the retina. Detachment of the retina has been reported in cases of congenital dislocation of the lens, even without operation,[19] and my colleagues and I have observed several such cases in the clinic of the Massachusetts Eye and Ear Infirmary. Certainly, the danger of subsquent detachment is greater if the extraction is complicated by loss of vitreous. It seems, therefore, that extraction of the lens is not to be recommended in these cases.

Discission of the lens in cases of congenital dislocation is notoriously difficult and unsatisfactory. Whereas in the normal lens wide opening of the anterior capsule results in prompt opacification, in the congenitally dislocated lens little, if any, opacity may develop, even after wide opening of the capsule. Furthermore, if the manipulations are too vigorous, there is danger of completely dislocating the lens with the needle. Discission with two needles has been advocated by Knapp[20]

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18. (*a*) Ringelhan, O., and Elschnig, A.: Über die Linsendislokationen, Arch. f. Augenh. **104**:325, 1931. (*b*) Marchesani, O.: Brachydaktylie und angeborene Kugellinse als Systemerkrankung, Klin. Monatsbl. f. Augenh. **103**:392, 1939. (*c*) Clarke, C. C.: Ectopia Lentis: A Pathologic and Clinical Study, Arch. Ophth. **21**:124 (Jan.) 1939. (*d*) Szinegh, B.: Zwei Fälle von beiderseitigen spontaner Linsenverlagerung bei kongenitaler Syphilis, Klin. Monatsbl. f. Augenh. **103**:230, 1939.

19. Ringelhan and Elschnig.[18a] Clarke.[18c] Burch, F. E.: Association of Ectopia Lentis and Arachnodactyly, Arch. Ophth. **15**:645 (April) 1936.

20. Knapp, A.: Operative Treatment of Congenital Subluxation of the Lens, Arch. Ophth. **27**:158 (Jan.) 1942.

and others.[21] The lens is fixed with one needle, while a thorough discission is done with the other. Even if this is done, repeated needlings may be necessary before an adequate pupillary opening in secured.

A simple method of discission which, so far as I know, has not been previously described, and which I have employed with satisfaction, is as follows: If, for instance, the lens is dislocated nasally, while the lens is fixed with one needle, the capsule is opened with a second needle and the lens stirred up as much as possible at the temporal equator of the lens. Since it is not the purpose of the operation to break up the lens completely, the manipulations may be gentle, and there is little danger of causing further dislocation of the lens. Though little opacification may occur, a shrinking of the lens takes place, thus enlarging the aphakic part of the pupil. In many cases a single needling done in this way may give an adequate aphakic pupil, even though three quarters of the lens is still intact. If after one such operation there is still an inadequate aphakic pupil, the operation is repeated in exactly the same way, the equator of the lens being again attacked. One should wait two or three months after each operation before undertaking another. In nearly all cases two such needlings provide an adequate aphakic pupil, and no further attempt need be made to get rid of the remainder of the lens.

In cases of microphakia or spherophakia the lens is of the same size and shape as in cases of congenital subluxation but is *in situ*. The same difficulties with operation are to be expected. Surgical intervention is, therefore, to be deferred until one can be absolutely sure that vision with best glass is too low for normal living. In many cases vision with a myopic correction will be found to be good enough that operation is not required. If corrected vision is so low that operation is necessary, discission is probably the method of choice.

If the lens is dislocated sufficiently in both eyes to permit aphakic vision with a small pupil, surgical intervention is not necessary. If aphakic vision is possible in one eye and in the second eye only phakic vision is possible, it may be well in some cases to forego operation on the second eye. The eye with aphakic vision may be used for distance, and the eye with phakic vision may be used for reading.

In cases of complete posterior dislocation, in which the lens is entirely out of the pupillary space, aphakic vision is possible, and no attempt should be made to remove the lens surgically. In some of these cases glaucoma will develop eventually, but chiefly, I believe, by the mechanism of pupillary block by vitreous. If the anterior chamber and the pupil are periodically inspected with the slit lamp for the presence of vitreous, one need have little fear of glaucoma. If at some time vitreous is seen protruding through the pupil into the anterior chamber, a peripheral transfixion of the iris should be done immediately to forestall glaucoma from pupillary block, if it has not already developed. In some of these cases detachment of the retina may develop, but the danger of this complication is definitely greater if the lens is removed surgically, always a formidable procedure.

In congenital dislocation of the lens and in microphakia, the lens may come into the anterior chamber. What is the mechanism by which the lens enters the anterior chamber? It does not simply fall into the anterior chamber by gravity,

21. Ringelhan and Elschnig.[18a] Wachtler, G.: Traumatische Luxation einer kongenitalen subluxierten Linse—Sekundärglaucom—Heilung von Katarakt und Glaukom durch Diszission, Klin. Monatsbl. f. Augenh. **91**:105, 1933.

for it may come into the anterior chamber even through the small pupil. In fact, in only rare instances is the pupil so large and the lens so small that it can pass freely in and out of the anterior chamber. The lens in congenital subluxation and microphakia is small and spherical. Owing to the action of centrifugal force or gravity, it comes against the back of the pupillary space, blocking the pupil; and, as pressure builds up in the posterior chamber, the pupil slowly dilates and the lens is gradually forced into the anterior chamber. This sequence of events was observed in its entirety by Dr. A. R. Irvine Jr. in a patient in a ward of the Massachusetts Eye and Ear Infirmary. The lens is seldom completely in the anterior chamber. As a rule, it is only partly in the anterior chamber and is gripped by the sphincter of the iris at its equator or somewhere behind the equator. In any case, the pupil is blocked and an acute rise of tension develops, with iris bombé. The glaucoma can be relieved immediately by transfixion of the iris. Dilation of the pupil likewise releases the blocked pupil, and the tension promptly falls. The use of miotics only aggravates the condition. If the lens has not been in contact with the cornea sufficiently long to become adherent, the lens goes back to its original position when the pupil is dilated, provided the zonule is not too severely damaged.

If the lens is in the anterior chamber and acute glaucoma ensues, what treatment should be employed? In nearly all reports [22] removal of the lens has been recommended. Doubtless this is the wisest treatment in most cases, but complications of such removal—detachment of the retina and atrophy of the globe [23]—are not infrequent and make the operation hazardous. There are instances, however, in which, if useful vision is possible when the lens is back in position and there is a relatively intact zonule, it would appear wiser to leave the lens in the eye and avoid the possible complications of removal. The lens can be prevented from again coming forward into the anterior chamber on subsequent occasions, not by the continued use of a miotic, although this has been recommended and has proved effective in some cases, at least for a time,[24] but by means of a prophylactic peripheral iridotomy or iridectomy. If a peripheral opening in the iris is present, the mechanism of pupillary block which causes the lens to be forced into the anterior chamber cannot occur. The question whether or not to remove the lens must be decided in each case on the basis of the findings. If slit lamp examination reveals that the zonule is largely lacking, the lens should be removed. If there is reason to suppose that the lens has been in the anterior chamber for some time, it may have become adherent to the cornea and must then be removed. Likewise, if it is known from previous examinations that vision with the lens in place is below a useful level, one should take the opportunity to remove the lens while it is in the anterior chamber.

22. Ringelhan and Elschnig.[18a] Marchesani.[18b] Clarke.[18c] Szinegh.[18d] Tupinambá, J.: Spontanluxation von beiden Linsen in die Vorderkammer, Rev. de oftal. de São Paulo **6**:13, 1938; abstracted, Zentralbl. f. d. ges. Ophth. **42**:571, 1938.

23. (*a*) Clarke.[18c] (*b*) Axenfeld, T.: Die Spontanluxation der durchsichtigen ektopischen Linse in die Vorderkammer, besonders im Kindesalter, und ihre operative Beiseitigung, Klin. Monatsbl. f. Augenh. **52**:195, 1914.

24. Luedde, W. H.: Indications for the Use of Pilocarpin in Dislocation of the Crystalline Lens: A Preliminary Report, Tr. Am. Ophth. Soc. **23**:71, 1925. Axenfeld.[23b]

If the lens is removed from the anterior chamber when the tension is high, there is much more danger of loss of vitreous, always a possible complication with this operation. It is wisest, therefore, to relieve the glaucoma by preliminary transfixion of the iris and then proceed with the extraction.

Occasionally a congenitally subluxated lens gradually loosens, from further tearing of the zonule, and over a period of time can be seen to shift its position. For the most part, such lenses gradually sink into the vitreous chamber but may sometimes come into the anterior chamber. When one observes such a shifting of the position of the lens taking place, it need not cause too great concern and does not necessarily demand immediate surgical intervention. In such a situation it is probably wiser to employ no treatment other than watchful waiting and to prescribe an aphakic correction when the pupil is clear.

SUMMARY AND CONCLUSIONS

Disorders of the lens in infancy and childhood requiring surgical treatment include congenital cataract, traumatic cataract, cataract associated with uveitis, congenital dislocation of the lens and microphakia. For each of these conditions, the indications for operation are discussed, factors concerning the choice of operation are considered and methods are suggested for the avoidance of the complications of surgery.

5 Bay State Road (15).

GLYCOLYTIC ACTIVITY OF THE CORNEA

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THERE are only a few scattered reports in the literature concerning the glycolytic activity of the cornea: Kohra [1] demonstrated considerable aerobic and anaerobic activity in various layers of the rabbit cornea. He also noted that in the presence of ischemia, produced by the ligation of the ciliary arteries, the metabolism of the whole cornea remained unchanged but the metabolism of the endothelium fell rapidly. Thus he concluded that the endothelium is more susceptible to change than the other layers of the cornea. Similar results were reported by Fischer,[2] though he failed to mention the type of experimental animal used or the technic employed. Herrmann and Hickman [3] described extensive studies on corneal metabolism, but their interest centered mainly on the effect of mustard gas (2-chloroethyl sulfide) on the cornea; subsequently, any results they obtained concerning glycolysis of the normal cornea were only incidental to their prime objective. Furthermore, their experiments were carried out at a temperature of 29 to 34 C. for 10 to 20 hours, during which time the possibility of bacterial contamination cannot be excluded. The latest communication in this field was that of Leinfelder,[4] who studied mainly the aerobic glycolysis of the rabbit cornea. Since the results reported by these authors vary considerably, it was thought advisable to investigate this problem thoroughly by studying both the aerobic and the anaerobic glycolysis of the normal bovine cornea.

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1. Kohra, T.: Über den Stoffwechsel der Hornhaut, Acta Soc. ophth. jap. **39**:1429, 1935.

2. Fischer, F. P., in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940.

3. Herrmann, H., and Hickman, F. H.: The Effect of Mustard on Some Metabolic Processes in the Cornea, Bull. Johns Hopkins Hosp. **82**:251, 1948; Studies on Physiology, Biochemistry, and Cytopathology of Cornea in Relation to Injury by Mustard Gas and Allied Toxic Agents: XII. Further Experiments on Corneal Metabolism in Respect to Glucose and Lactic Acid, ibid. **82**:260, 1948; X. Exploratory Studies on Corneal Metabolism, ibid. **82**:225, 1948.

4. Leinfelder, P. J.: Aerobic Glycolysis of Corneal Tissue, Tr. Am. Ophth. Soc. **46**:412, 1948.

I. ANAEROBIC GLYCOLYSIS

The first part of this study will be concerned with the following aspects of the problem:

1. The anaerobic glycolysis of various corneal layers.

2. The anaerobic glycolysis of the damaged corneal epithelium.

3. Ability of the cornea to produce lactic acid anaerobically in the absence of glucose, and the possible source of lactic acid under such conditions.

4. The influence of environment, especially the hydrogen ion concentration (p_H), on the anaerobic glycolysis of the cornea.

Technic.—The conventional Warburg manometric method, as described by Dixon,[5] was used. Flat-bottomed flasks, without center wells, were employed; one fresh beef cornea, cut into quadrants, was placed in each flask, which contained Krebs's[6] medium 1, without the organic acids. This suspension medium contained NaCl, KCl, CaCl, KH_2PO_4 and $MgSO_4$ and was buffered with $NaHCO_3$. The flasks were gassed with a mixture of 5 per cent carbon dioxide and 95 per cent nitrogen, and the experiment was conducted at 37 C. for one to two hours, readings being taken at 15 minute intervals. Some of the flasks contained metabolites, such as glucose or pyruvate, in various concentrations. In a few experiments the substrate was placed in the side arm of the flask and tipped into the main compartment at stated intervals. After the experiment the corneas were dried to constant weight at 105 C. and the results expressed in terms of dry weight. To study the anaerobic glycolysis of various corneal layers, the epithelium was scraped off with a scalpel and transferred directly into reaction flasks, the epitheliums from two corneas being used for each flask. In another series of experiments the scraped-off epitheliums were pooled and homogenized, as described in a previous communication,[7] and then aliquot portions of the homogenate were pipetted into the flasks. The dry weight of this scraped-off and/or homogenized epithelium was estimated to be 20 per cent of the wet weight. The remaining stroma was also utilized, with or without endothelium.

Since this conventional manometric method measures only evolution of carbon dioxide and presupposes that the acid produced is lactic acid, it was thought advisable to check the results with direct determinations of lactic acid. The Barker-Summerson[8] method was employed, which is highly specific for lactic acid. Two flasks containing halves of each of two corneas were used; in the first flask the "initial" amount of lactic acid was determined after equilibration, and in the second flask the "final" amount of lactic acid was obtained at the end of the experiment, thus enabling the calculation of the amount of acid produced over the experimental period. Every alternate manometric experiment was checked with the direct chemical determination.

In one set of experiments the p_H of the suspension medium was varied from 6.4 to 8.0 by using more or less $NaHCO_3$ but maintaining the same carbon dioxide-nitrogen mixture for the gassing; i. e., utilizing the Henderson-Hesselbach equation, as described by Umbreit and associates.[9]

Results.—Since the results of the manometric method and the direct chemical determinations agreed to within less than 10 per cent, it was decided to express all results in terms of evolution of carbon dioxide, microliter of carbon dioxide being equivalent to 4 micrograms of lactic acid.

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5. Dixon, M.: Manometric Methods as Applied to the Measurement of Cell Respiration and Other Processes, ed. 2, London, Cambridge University Press, 1943.

6. Krebs, H. A.: Body Size and Tissue Respiration, Acta biochim. et biophys. **4**:249, 1950.

7. deRoetth, A., Jr.: Respiration of the Cornea, Arch. Ophth. **44**:666 (Nov.) 1950.

8. Barker, S. B., and Summerson, W. H.: The Colorimetric Determination of Lactic Acid in Biological Material, J. Biol. Chem. **138**:535, 1941.

9. Umbreit, W. W.; Burris, R. H., and Stauffer, J. F.: Manometric Techniques and Tissue Metabolism, Minneapolis, Burgess Publishing Company, 1949.

Table 1 shows that the $Q^{N}_{CO_2}$ (microliters of carbon dioxide liberated under anaerobic conditions per milligram dry weight tissue per hour) without added glucose was + 0.70, + 0.181 and + 0.110 for the whole cornea, the endothelium and stroma, and the stroma alone, in that order. However, if glucose was added to the suspending medium, so that the concentration was 100 mg. per 100 cc., the carbon dioxide production of the whole cornea was doubled, while that of the endothelium and stroma and of the stroma alone was approximately tripled.

TABLE 1.—*Anaerobic Glycolysis of Whole Bovine Cornea, Isolated Endothelium and Stroma, or Stroma Alone, Expressed in Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour, Each Figure Representing One Cornea*

	Whole Cornea		Endothelium and Stroma		Stroma Alone	
	Control	Glucose, 100 Mg./ 100 Cc.	Control	Glucose, 100 Mg./ 100 Cc.	Control	Glucose, 100 Mg./ 100 Cc.
	+ 0.58	+ 1.40	.....	.....	.....	.....
	+ 0.60	+ 1.35	.....	.....	.....	.....
	+ 0.78	+ 1.24	.....	.....	.....	+ 0.30
	+ 0.78	+ 1.58	.....	.....	.....	+ 0.28
	+ 0.72	+ 1.43	+ 0.212	+ 0.54	+ 0.09	+ 0.17
	+ 0.78	+ 1.42	+ 0.150	+ 0.51	+ 0.11	+ 0.18
	+ 0.66	+ 1.45	+ 0.180	+ 0.52	+ 0.14	+ 0.30
	+ 0.71	+ 1.40	+ 0.182	+ 0.44	+ 0.10	+ 0.20
	+ 0.76	+ 1.22	+ 0.173	+ 0.51	+ 0.11	+ 0.27
	+ 0.63	+ 1.43	+ 0.188	+ 0.58	+ 0.10	+ 0.30
Average	+ 0.70	+ 1.40	+ 0.181	+ 0.52	+ 0.11	+ 0.25

TABLE 2.—*Anaerobic Glycolysis of Bovine Corneas in Presence of Varying Concentrations of Added Glucose, Expressed in Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour, Each Figure Representing One Whole Cornea*

	Glucose/100 Cc.			
Control	20 Mg.	50 Mg.	100 Mg.	200 Mg.
+ 0.74	+ 1.07	+ 1.22	+ 1.43	+ 1.34
+ 0.64	+ 1.19	+ 1.26	+ 1.22	+ 1.35
+ 0.70	+ 1.12	+ 1.21	+ 1.24	+ 1.30
+ 0.60	+ 1.10	+ 1.28	+ 1.40	+ 1.40
Average + 0.66	+ 1.12	+ 1.24	+ 1.33	+ 1.35

The results in table 2 illustrate that even a small amount of glucose, such as 20 mg. per 100 cc. in final concentration, increased the acid production to almost the same level as the 50, 100 or 200 mg. per 100 cc. concentration. It can also be seen that raising the glucose concentration above 50 mg. per 100 cc. did not increase the rate of anaerobic glycolysis. Control experiments also demonstrated that the rate of carbon dioxide production was raised to the same level regardless of whether the glucose was added at the beginning of the experiment or after 30 minutes of anaerobic glycolysis.

Table 3 A shows that the scraped-off, but not homogenized, corneal epithelium has a $Q^{N}_{CO_2}$ of + 3.5, which is increased to + 4.4 in the presence of glucose; pyruvate, however, had no effect on the anaerobic glycolysis of the corneal epithelium.

The effect of homogenization on the anaerobic acid production of the corneal epithelium is illustrated in table 3 B. Without added glucose the rate of carbon dioxide production fell off rapidly after the first 30 minutes, but addition of glucose to a final concentration of 100 mg. per 100 cc. steadied and maintained the carbon dioxide evolution at a high rate for at least one hour. If one calculates results from the steepest slope of the activity-time curve, the $Q^{N}_{CO_2}$ of the homogenized epithelium was approximately doubled in the presence of glucose. Pyruvate, on

TABLE 3.—*Anaerobic Glycolysis of Corneal Epithelium, Expressed in Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour, Each Figure Representing Pooled Epithelium Obtained from Two Bovine Corneas*

	Control	Glucose, 100 Mg./100 Cc.	Pyruvate, 10 Mg./100 Cc.
A. Isolated, Scraped-Off Corneal Epithelium			
	+3.6	+4.4	.....
	+2.1	+4.5	+3.2
	+3.9	+5.4	.....
	+4.0	+4.2	+4.1
	+3.0	+4.8	.....
	+4.4	+4.8	+3.0
	+3.6	+4.2	+3.3
	+4.1	+4.5	.....
Average	+3.6	+4.6	+3.4
B. Homogenized Corneal Epithelium			
Exper. No.			
1 (12 eyes)	+0.65	+1.61	+1.02
2 (15 eyes)	+1.54	+2.78	+1.49
3 (15 eyes)	+0.70	+1.74	+1.00
4 (20 eyes)	+1.80	+3.00	+1.09
Average	+1.17	+2.28	+1.15

TABLE 4.—*Anaerobic Glycolysis of Fifteen Bovine Corneas, Expressed in $Q^{N}_{CO_2}$ Units (Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour), Following Changes in p_H of Suspending Medium*

p_H	$Q^{N}_{CO_2}$				p_H	$Q^{N}_{CO_2}$		
6.4	+0.33	+0.30	+0.26	+0.24	7.2	+0.98	+0.80	.....
6.6	+0.44	+0.47	.....	.....	7.5	+1.20	+1.42	+1.48
6.8	+0.51	+0.48	.....	.....	8.0	+1.75	+1.67	.....

the other hand, did not influence the anaerobic glycolysis of the homogenized epithelium. As a control experiment, it was also demonstrated that pyruvate did not affect the anaerobic acid production of the whole cornea.

Varying the p_H of the suspension medium, as seen in table 4, had a considerable effect on the anaerobic acid production of the cornea; below p_H 7.4 to 7.6, which is the average p_H of the extracellular fluids, the carbon dioxide evolution was distinctly suppressed, while above this range it was accelerated.

Comment.—The results of this series of experiments showed that the three corneal layers studied, i. e., the epithelium, the stroma and the endothelium, have measurable anaerobic glycolytic activities. Glucose markedly increased the anaerobic acid production of the cornea, and even a small amount of glucose, 20 mg. per 100 cc., was sufficient to raise the carbon dioxide production rate appreciably. It

was observed that the per cent increase in glycolysis (not the absolute amount) following addition of glucose was greater in the endothelium and stroma, as well as in the stroma alone, than it was in the whole cornea. Previous experiments [10] conducted in this laboratory showed that the corneal epithelium has a considerably higher content of readily available carbohydrates than the rest of the cornea. Therefore it appears reasonable to assume that the increased anaerobic glycolysis following addition of glucose would be less pronounced in the whole cornea than in the endothelium and stroma.

The anaerobic glycolysis of the homogenized epithelium was lower than that of the scraped-off epithelium, which, in turn, was less than the theoretical value for the intact epithelium, calculated from the $Q^{N}_{CO_2}$ of the whole cornea minus that of the endothelium and stroma. Similar results were noted also in connection with the oxygen uptake measurements reported in a previous communication.[7] These experiments indicate that any mechanical disturbance of the corneal epithelium, such as scraping it off the stroma or homogenizing it, greatly depresses its metabolic activity. Therefore these procedures are contraindicated if one intends to study the metabolism of the corneal epithelium under optimum physiological conditions.

If one compares the anaerobic glycolysis of the scraped-off epithelium with that of the homogenized epithelium, it can be noticed that, while the final results vary considerably, the difference between the control group and the glucose-containing group is approximately the same in these two experiments. This means that the "endogenous" anaerobic glycolysis, i. e., the anaerobic glycolysis of the tissue without extra glucose, was considerably less in the case of the homogenized epithelium than in the case of the scraped-off epithelium. On the other hand, the "exogenous" anaerobic glycolysis, i. e., the amount of glycolysis due to the added glucose, was identical in the two experiments. This phenomenon can be explained if one assumes that the substrate for the endogenous glycolysis was not glucose, but some other carbohydrate, such as glycogen. During the homogenization procedure the glycogen of the epithelium diffuses into and is diluted with the suspension fluid; thus its concentration falls below the minimum necessary to saturate the enzyme system responsible for its breakdown. In the case of the scraped-off corneal epithelium, however, this dilution factor does not come into consideration; therefore the enzyme system remains saturated with glycogen. If glucose is added to the suspending medium, its concentration remains the same whether the epithelium is homogenized or only scraped off; therefore the enzyme responsible for glucose breakdown is saturated in both procedures. Thus it can be concluded that the enzyme system responsible for the glycogen breakdown was more affected by the homogenization than by the scraping procedure, while the enzyme causing the glucose breakdown was influenced by both procedures to the same extent.

The influence of p_H on the anaerobic glycolysis of the cornea, showing an increased acid production with a corresponding increase in the p_H, is of special interest, since it was previously demonstrated that oxygen uptake of the cornea was not affected with variation in the p_H of the suspension medium. A review of the literature reveals that, while in most mammalian tissues oxygen uptake is greatly influenced by changes in the p_H of the suspending medium, there are a few

10. deRoetth, A., Jr.: Unpublished data.

tissues [11] which are reported to show this peculiar metabolic phenomenon demonstrated by the cornea, i. e., a change in p_H not affecting oxygen uptake, but markedly influencing anaerobic glycolysis.

It is interesting to note that a metabolite other than glucose, i. e., pyruvate, did not influence the anaerobic glycolysis of the whole cornea or of the isolated epithelium.

AEROBIC GLYCOLYSIS

The second part of this study will be concerned with the following problems:

1. The aerobic glycolysis of various corneal layers, both in the presence and in the absence of glucose.

2. The effect of changes in the p_H of the suspending medium on the aerobic glycolysis of the cornea.

3. The influence of mechanical injury on the aerobic glycolysis of the corneal epithelium and on the stroma.

Technic.—The procedure employed was essentially the same as that used for the anaerobic experiments, with a few alterations. Naturally, the gas used was a mixture of 5 per cent carbon dioxide and 95 per cent oxygen. In one experiment the epithelium was scraped off, and the remaining endothelium and stroma, plus the scraped-off epithelium, were placed in the same Warburg flask and aerobic glycolysis was determined manometrically. In this case the dry weight of the scraped-off epithelium, which was estimated to be 20 per cent of the wet weight, was added to the determined dry weight of the rest of the cornea. In order to study the effect of mincing on the aerobic glycolysis of the stroma, several corneas minus their epithelium and endothelium were pooled. The stroma was cut into small pieces with scissors, and then weighed aliquot portions were placed in the flasks. In order to determine the limitations of oxygen diffusion due to the thickness of the corneal stroma, a number of corneal stromas were split into halves with a sharp scalpel or cut into several sections with a tissue slicer.

Results.—The indirect manometric method is less accurate for the study of aerobic glycolysis than for anaerobic glycolysis, because one has to assume that the respiratory quotient of the tissue to be studied is 1.00. Therefore the direct chemical determinations of lactic acid are more specific in this case, and thus the accompanying tables show the results of both the manometric and the direct chemical methods. $Q^{M}_{CO_2}$ denotes the microliters of carbon dioxide liberated per milligram of dry weight tissue per hour, and $Q^{O_2}_{L}$ signifies the micrograms of lactic acid produced according to the direct chemical method per milligram of dry weight per hour. One microliter of carbon dioxide is equivalent to 4 micrograms of lactic acid. The inaccuracy of the indirect manometric method is illustrated by the fact that this 1 : 4 ratio did not always occur in the present study.

Table 5 shows that in the presence of glucose the $Q^{L}_{O_2}$ of the whole cornea, the endothelium and stroma, and the stroma alone was + 1.41, + 1.40 and + 0.88, respectively. Without added glucose there was no demonstrable aerobic glycolysis in these tissues, either with the manometric or with the chemical method.

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TABLE 5.—*Aerobic Glycolysis of Whole Cornea, Endothelium and Stroma, and Stroma Alone in Presence of 100 Mg./100 Cc. of Glucose, Expressed in Terms of Microliters of Carbon Dioxide Produced per Milligram Dry Tissue per Hour ($Q^{M}_{CO_2}$ = Manometric Method), or in Terms of Micrograms of Lactic Acid Produced per Milligram Dry Tissue per Hour ($Q^{O_2}_{L}$ = Direct Chemical Method), Each Figure Representing One Bovine Cornea*

	Whole Cornea				Endothelium and Stroma				Stroma Alone			
	Control	$Q^{M}_{CO_2}$ Glucose, 100 Mg./ 100 Cc.	Control	$Q^{O_2}_{L}$ Glucose, 100 Mg./ 100 Cc.	Control	$Q^{M}_{CO_2}$ Glucose, 100 Mg./ 100 Cc.	Control	$Q^{O_2}_{L}$ Glucose, 100 Mg./ 100 Cc.	Control	$Q^{M}_{CO_2}$ Glucose, 100 Mg./ 100 Cc.	Control	$Q^{O_2}_{L}$ Glucose, 100 Mg./ 100 Cc.
	0	+0.30	0	1.14	0	+0.35	0	1.42	0	+0.11	0	0.81
	0	+0.20	0	1.07	0	+0.20	0	1.30	0	+0.19	0	0.67
	0	+0.22	0	1.30	0	+0.28	0	1.05	0	+0.14	0	0.65
	0	+0.27	0	1.27	0	+0.26	0	0.84	0	+0.18	0	0.81
	0	+0.37	0	1.73	0	+0.27	0	1.45	0	+0.40	0	1.04
	0	+0.24	0	2.00	0	+0.37	0	1.62	0	+0.22	0	1.00
	0	+0.21	0	1.00	0	+0.40	0	1.85	0	+0.26	0	1.00
	0	+0.20	0	1.18	0	+0.27	0	1.70	0	+0.28	0	1.08
Average..	0	+0.25	0	1.41	0	+0.31	0	1.40	0	+0.22	0	0.88

TABLE 6.—*Aerobic Glycolysis of Cornea in Presence of 100 Mg./100 Cc. Glucose Following Changes in p_H of Suspending Medium, Expressed in $Q^{M}_{CO_2}$ Units (Microliters of Carbon Dioxide Produced Manometrically per Milligram Dry Weight Tissue per Hour) or in $Q^{O_2}_{L}$ Units (Micrograms of Lactic Acid Produced According to the Direct Chemical Method per Milligram Dry Weight Tissue per Hour), Each Figure Representing One Bovine Cornea*

p_H	$Q^{M}_{CO_2}$	$Q^{O_2}_{L}$	p_H	$Q^{M}_{CO_2}$	$Q^{O_2}_{L}$
6.4	0	0	7.5	+0.28	1.30
	0	0		+0.21	1.27
6.8	0	0	8.0	+0.40	2.00
	0	0		+0.38	2.24
7.2	+0.06	+0.54			
	+0.06	+0.75			

TABLE 7.—*Aerobic Glycolysis of Corneal Epithelium Expressed in Microliters of Carbon Dioxide Liberated per Milligram Dry Weight Tissue per Hour, Each Figure Representing Epithelium from Two Bovine Corneas*

	Control	Glucose, 100 Mg./100 Cc.	Pyruvate, 10 Mg./100 Cc.
A. Scraped-Off Corneal Epithelium			
	+2.41	+2.41	.....
	+2.81	+2.81	.....
	+1.90	+3.00	+1.9
	+1.70	+3.10	+1.7
	+2.0	+2.5	+2.0
	+1.9	+3.2	+2.2
	+2.3	+2.9	+1.4
	+1.8	+2.9	+1.8
Average	+1.9	+2.8	+1.8
B. Pooled, Homogenized Epithelium			
Exper. No.			
1 (20 eyes).....	+0.96	+2.85	+1.11
2 (12 eyes).....	+0.80	+0.86	+0.98
3 (20 eyes).....	+0.67	+1.31	.....
4 (20 eyes).....	+1.82	+2.71	.....
Average	+1.06	+1.93	+1.04

Table 6 demonstrates that at a low p_H (6.4 to 6.8) aerobic acid formation of the cornea was completely suppressed, while at a higher p_H (8.0) it was noticeably accelerated. This increased aerobic glycolysis due to increase in the p_H of the suspension medium is manifested by many mammalian tissues.

Both the scraped-off and the homogenized corneal epithelium showed a marked aerobic glycolysis (table 7), which was somewhat increased in the presence of added glucose but was not affected by pyruvate. This experiment illustrated the fact that the "exogenous" aerobic glycolysis was the same both in the scraped-off and in the homogenized corneal epithelium; similar results were noted also in the anaerobic experiments.

TABLE 8.—*Aerobic Glycolysis of Scraped-Off Corneal Epithelium, Together with Rest of Same Cornea, Expressed in Terms of Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour*

	Control	Glucose, 100 Mg./100 Cc.
	+0.32	+0.76
	+0.45	+0.69
	+0.30	+0.66
	+0.38	+0.59
	+0.44	+0.72
	+0.35	+0.67
Average	+0.39	+0.68

TABLE 9.—*Aerobic Glycolysis of Macerated or Minced Corneal Stroma, in Presence of 100 Mg./100 Cc. Glucose, Expressed in $Q^{M}_{CO_2}$ Units (Microliters of Carbon Dioxide Produced per Milligram Dry Weight Tissue per Hour) or in Terms of $Q^{O_2}_{L}$ Units (Micrograms of Lactic Acid Produced per Milligram Dry Weight Tissue per Hour), Each Figure Representing Stroma from Two Bovine Corneas*

Sliced Stroma		Minced Stroma	
$Q^{M}_{CO_2}$	$Q^{O_2}_{L}$	$Q^{M}_{CO_2}$	$Q^{O_2}_{L}$
−0.20	0.88	0	0
−0.12	1.00	0	0
−0.30	0.90	0	0
−0.22	0.80	0	0

Table 8 shows that the aerobic glycolysis of the scraped-off epithelium plus the remaining endothelium and stroma was considerably higher than when the epithelium was left intact on the cornea. Also, one can notice that in this experiment aerobic acid formation was elicited even in the absence of glucose, while in the case of the intact, whole cornea this never occurred.

Table 9 demonstrates that there was no appreciable difference in the aerobic glycolysis of the sliced stroma and that of the whole stroma, indicating that the thickness of the stroma was not a limiting factor in the diffusion of oxygen into the tissue. Mincing of the stroma, however, completely inhibited its aerobic glycolytic activity.

Comment.—The most significant finding in this study is that the normal corneal epithelium in situ, i. e., while on the cornea, apparently does not have a measurable aerobic glycolysis. This conclusion may be obtained from the fact that the aerobic

glycolysis of the whole cornea and that of the endothelium and stroma were the same. However, even a relatively slight injury, such as the separation of the epithelial layer from the rest of the cornea, will produce aerobic glycolysis in the epithelium. The high aerobic glycolytic activity of the scraped-off and homogenized epithelium can be explained by the damage done to the epithelium during this crude mechanical procedure. It is generally believed that many actively metabolizing tissues manifest aerobic glycolysis only on injury, such as that produced by slicing, cutting or homogenizing.

The intact endothelium, however, does have an aerobic glycolysis, since the acid production of the endothelium and stroma was consistently higher than that of the stroma alone.

At this time attention should be brought to Leinfelder's [4] conclusion that the cornea does not show aerobic glycolysis in the absence of glucose because in this case the carbon dioxide liberated is bound to the cornea. The present study substantiates Leinfelder's results in so far as it proves that the cornea does not have an aerobic glycolysis in the absence of glucose, but it differs regarding the carbon dioxide retention. If the liberated carbon dioxide were retained by the tissues, as reported by Leinfelder, then the direct chemical method would show lactic acid production. That this was not the case was demonstrated by the fact that even the direct chemical determination showed a complete lack of lactic acid production in the absence of glucose.

If one compares the aerobic with the anaerobic glycolysis, several interesting observations may be made. In the first place, it can be seen that the intact normal corneal epithelium has a pronounced anaerobic, but no aerobic, glycolysis, a condition typical of many actively metabolizing tissues. The corneal stroma, on the other hand, manifests approximately identical aerobic and anaerobic glycolytic activities. A similar type of glycolysis was reported to be present in the articular cartilage [12]; indeed, the corneal stroma and the articular cartilage show several similarities. They both are connective tissues of mesenchymal origin, with relatively low metabolic activity; also, they both are relatively homogeneous tissues containing mainly one type of cell. There are reports in the literature that the skin [13] and the intestinal mucosa [14] produce lactic acid aerobically. In the light of the knowledge obtained from this study, it can be assumed that the aerobic glycolysis manifested by these tissues is probably due entirely to their connective tissue layers, and that their intact epithelial layers normally do not produce lactic acid aerobically. How-

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ever, it would be difficult to prove this assumption, because accurate anatomic separation of the epithelium from the connective tissue is difficult in the case of the skin and intestinal mucosa. Research on the various aspects of cellular metabolism was always hampered by the fact that most mammalian tissues cannot be separated accurately into their various tissue layers. Thus, the cornea may be considered an excellent model for the study of glycolysis of a complex tissue, since with relative ease one can separate it into its main component layers.

These experiments are of general physiological interest, for, taking the cornea as an example, one can arrive at certain conclusions concerning the metabolism of connective and epithelial tissues in general. It seems reasonable to assume that the metabolically active epithelial tissues in general probably do not glycolyze aerobically when they are left intact; however, even the slightest injury, such as their removal from their supporting connective tissue base, causes them to produce lactic acid aerobically. Connective tissues, on the other hand, even if they are not damaged, glycolyze aerobically.

SUMMARY

The intact corneal epithelium was demonstrated to have a considerable anaerobic, but no aerobic, glycolysis; the injured corneal epithelium, on the other hand, showed a pronounced aerobic glycolysis, which is characteristic of a metabolically active tissue.

In the case of the corneal stroma the rate of anaerobic acid production was the same as that of the aerobic, a condition typical of metabolically inactive tissues.

An increase in the p_H of the suspension medium was paralleled by an increase in the glycolytic activity of the cornea.

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This study was carried out under the guidance of Dr. Zacharias Dische.

EXPERIMENTAL STUDIES ON EARLY LENS CHANGES AFTER ROENTGEN IRRADIATION

I. Morphological and Cytochemical Changes

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SINCE it was first shown that roentgen ray cataract could be produced experimentally in mature animals (in guinea pigs by Bossuet,[1] in 1909, and in rabbits by Aulamo,[2] in 1928), the question of the primary site of radiation injury to the lens and the pathogenesis of the lesion have been discussed by many investigators on the basis of experimental and clinical evidence and have been studied systematically by a few. Most investigators have favored the concept of direct radiation damage to the lens (Bossuet,[1] Politzer,[3] Rohrschneider,[4] Peter,[5] Grzedzielski,[6] Okusawa,[7] Leinfelder and Kerr,[8] Goldmann and Liechti,[9] von Szily,[10] Krückmann,[11]

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(Footnotes continued on next page)

Poppe [12]), whereas others, on the basis of the clinical characteristics of the cataract, have preferred the hypothesis of an indirect radiation effect induced by damage to the structures of the ciliary processes, with consequent nutritional disturbance of the lens (Aulamo,[2] de Schweinitz,[13] Stallard,[14] Milner,[15] Woelfflin [16]). A third group of authors have failed to express themselves clearly on this point (Lebensohn,[17] Clapp,[18] Taliercio [19] and others).

According to the theory of direct radiation effects on the lens, the initial lesion has been thought to be present either in the germinative zone of the lenticular epithelium (an opinion shared by the great majority of workers) or, on the basis of clinical observations, in the lens fibers in the axial part of the cortex (Peter and Vogt [20]). Politzer [3] considered that early alterations in the permeability of the lens capsule played an important part in the development of the cataract he produced in salamander larvae with roentgen radiation. For obvious reasons, not much information on the sequence of early changes and their causative interrelation could be expected from histological examination of human lenses with radiation cataract (Rohrschneider,[4] Grzedzielski,[6] Leinfelder and Kerr,[8] Reese,[21] Krückmann [11]). By the time such lenses were submitted for microscopic examination, long after radiation had been completed, they showed advanced stages of cataract formation, and artefacts from the trauma of intercapsular extraction could also have confused the histological picture. The interpretations could thus only be conjectured from the clinical course and experimental data. As for biomicroscopic examination, it should be remembered that the periphery of the lens is not usually accessible to the biomicroscope.

Outstanding experimental contributions to the problem have been made more recently by Leinfelder and Kerr,[8] Goldmann and Liechti [9] and Poppe.[12] Poppe used one standard irradiation technic and studied microscopically the initial changes in a large number of experimental animals. Applying a histological technic similar

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21. Reese, A. B.: Operative Treatment of Radiation Cataract, Arch. Ophth. **21**:476 (March) 1939.

to that devised by Verhoeff, Bell and Walker [22] for studies of the effects of ultraviolet radiation on the lens, he used flat preparations of the anterior capsule with the adherent lens epithelium.

Observation of Poppe's technic in this laboratory indicated that artefacts due to stretching and drying could not be avoided with certainty, that examination of the epithelium in the preequatorial zone was often unsatisfactory and that examination of the lens bow and fibers was impossible. A compensatory advantage, however, lay in the high magnification which could be used in analyzing cytological changes.

In the present study flat preparations of the lens epithelium were utilized to observe and quantitate early cytochemical changes in the cell nuclei of irradiated eyes. It is known to pathologists, and is also evident from Poppe's photomicrographs, that meridional sections of an entire rabbit lens leaves much to be desired. Since this is the type of section to be preferred for the purpose of alining morphological with cytochemical changes, the usual technic was modified for use in the present study so that paraffin sections about 5 microns thick could be obtained. This modification also permitted cell counts to be made in the germinative area of the epithelium under standard conditions and facilitated the observation of early changes in the cytoplasm of the fibers, as well as in the nuclei.

METHODS OF STUDY

Irradiation Technic.—In the main series of experiments, 59 chinchilla rabbits (71 eyes) were subjected to one type of irradiation technic. A single dose of 2,000 r of penetrating roentgen rays was administered. The radiation factors were as follows: 220 kv.; 20 ma.; 145 r per minute in air; 0.5 mm. Cu + 1 mm. Al filtration; 30 cm. target skin distance; 20 mm. field (round); half-value layer, 1 mm. Cu. The animals, under pentobarbital sodium anesthesia, were fastened to the board so that one eye of each animal could be irradiated while the other, shielded, remained outside the beam. The upper lid of the eye to be irradiated was held open with Scotch tape and the roentgen ray beam directed from above. In 53 rabbits the upper limbus was centered in the field and the margin of the lids kept within the field; in 6 rabbits the beam was alined with the optical axis. One operator watched continuously the position of the animal's head. In an additional series of 17 rabbits (23 eyes) a dose of 1,000 r was used twice, the second dose being given either one week or three weeks after the first. Repeated observations with focal illumination, with the biomicroscope and with the ophthalmoscope were made at intervals ranging from 24 hours to two weeks over observation periods varying in length up to one year.

Histological Technic.—The lenses were freed cautiously from the attachments in the equatorially opened globes and during the procedure were fixed by the injection of Carnoy solution (1 part glacial acetic acid and 3 parts 95 per cent alcohol). Traction on the zonula was avoided. From the fixed lens a large calotte of the posterior cortex in the form of a round disk was then removed. It contained the entire horizontal suture. The peripheral part of the posterior cortex, with the rest of the equatorial area, remained uninjured. Through the opening in the posterior cortex the nucleus was delivered by being carefully separated from the surrounding cortex with a fine spatula. The preparations of the experimental and control lenses, consisting of the intact anterior cortex, the equator of the lens and the peripheral portion of the posterior cortex, were then treated according to Stowell's [23] technic recommended for studies of desoxyribonucleic acid with the Feulgen reaction in paraffin sections. The preparations of the irradiated and the normal lenses were embedded in the same block, cut in the direction of the vertical meridian in 5 micron sections and mounted and stained together on the same slide.

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23. Stowell, R. E.: Feulgen Reaction for Thymonucleic Acid, Stain Technol. **20**:45, 1945.

The posterior calottes of the experimental and control preparations were also treated together and sectioned perpendicular to the horizontal suture. Fifteen irradiated and 15 control lenses were prepared for examination in this manner. For flat preparations of the lens epithelium, Poppe's [12] method was followed, with minor modifications. They will be mentioned in the paragraph on staining technic.

Staining Technic.—From each pair of lenses groups of from eight to 10 slides, each with three or four pairs of sections, were stained (1) with hematoxylin and eosin, (2) according to Stowell's modification of the Feulgen technic, (3) with methyl green, and (4) with methyl green and pyronin. Methyl green, of the National Aniline Company, was purified with chloroform, and the pyronin was recrystallized several times before being put in solution. The slides were stained for 45 minutes at 56 C. and washed quickly in ice water. After gentle blotting, they were differentiated for 24 hours in tertiary butyl alcohol, cleared in xylol and mounted in clarain (clarite®). In contrast to the Feulgen stain, methyl green indicates with alleged specificity the degree of polymerization of desoxyribonucleic acid (Brachet,[24] Kurnick,[25] Pollister and Leuchtenberger)[26]. The second basic dye, pyronin, is thought to designate the content of ribonucleic acid in the cytoplasm.

The Feulgen reaction and the methyl green technic were employed on flat preparations after they had been fixed in Carnoy's solution. Prior to this step, a thin layer of the fixative was spread on chemically clean slides, and the properly incised lenses were placed there. After removal of the nucleus and cortical matter, the slides were transferred to the fixing solution and left there for one hour. The fixation could not precede the dissection of the lens because such a procedure prevented the smooth separation of the fibers from the epithelium. Instillation of an 0.9 per cent solution of sodium chloride during the process of freeing the lens from its attachments minimized the drying effects. The various steps in dehydration and performance of the specific reaction were analogous to those described by Stowell for paraffin sections.

A quantitative estimation of the two cytochemical reactions used was attempted by applying the technic described by Gomori [27] for the quantitation of enzyme reactions. Tracings on Coujard slides with serial dilutions of a pure and highly polymerized desoxyribonucleic acid showed after completion of the reaction varying intensities of staining, dependent on the concentrations employed. Whereas the methyl green gave a relatively homogeneous staining of the inscriptions on the slide, the value of the technic appeared questionable for the Feulgen reaction because of unpredictable precipitations of the colored compound. The use of such reference slides was limited therefore to the methyl green reaction, i. e., to the semiquantitative evaluation of the polymerization of desoxyribonucleic acid in the cell nuclei of irradiated and control lenses. Since these control lenses were exposed possibly to an indirect irradiation of about 7 r, the experimental series included also comparative examinations with material from nonirradiated animals of the same age group. Preparations were made from the lenses at the end of three hours, one day, three days, one week, two weeks and longer intervals after irradiation.

EXPERIMENTAL RESULTS AND COMMENT

Morphological Changes

In Vivo Observations.—In 53 of the 56 irradiated eyes observed longer than a month, clinically recognizable changes occurred from four to 10 weeks after irradiation. At this time there first appeared in the periphery close to the equator of the lens a fine, slightly irregular, dark ring, which could be seen ophthalmo-

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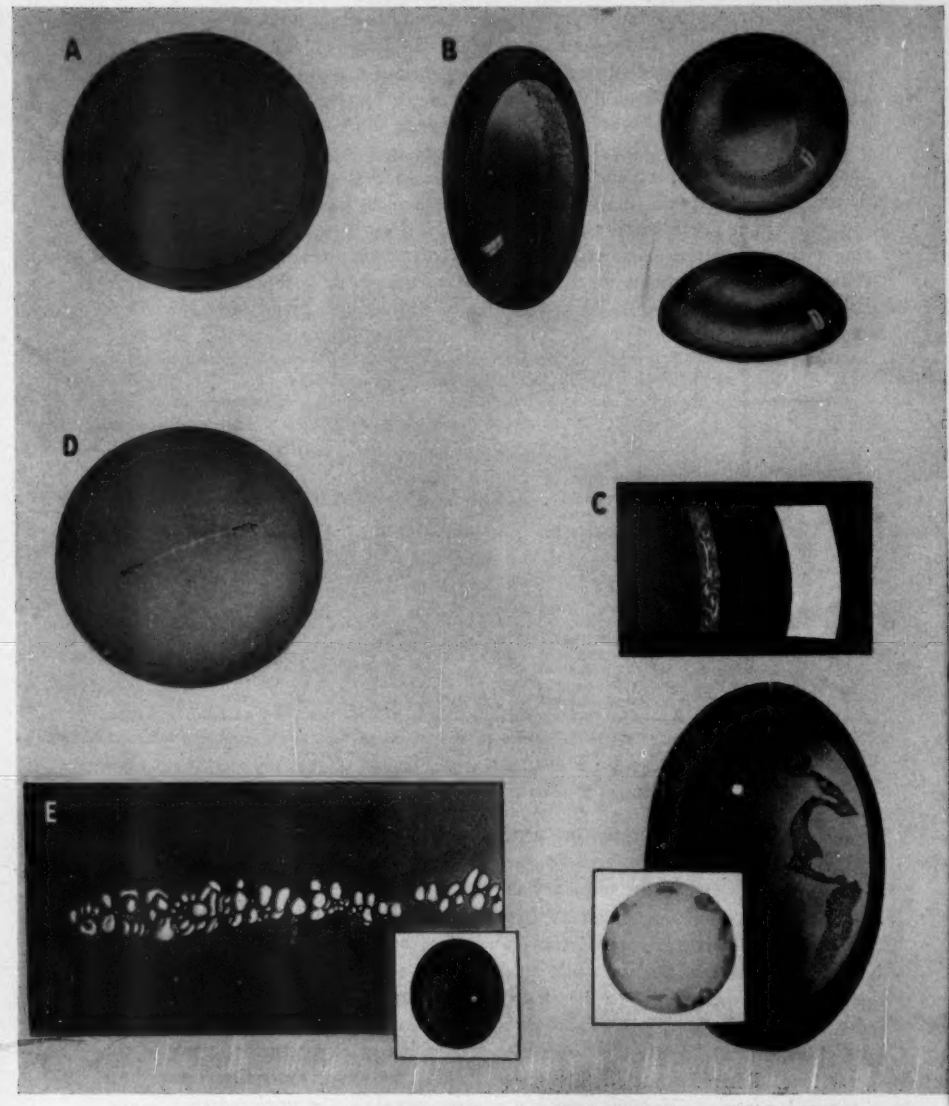

Fig. 1.—*A*, equatorial opacity and vacuoles at posterior cortex. *B*, equatorial opacity and ring of vacuoles between periphery and central part of posterior cortex. *C*, mosslike opacity beneath anterior capsule of lens, with vacuoles in garland pattern between periphery and central part of posterior cortex. *D* and *E*, vacuoles at posterior suture five weeks after irradiation.

scopically when the pupil was dilated maximally with atropine and phenylephrine. The granular texture of the opacity permitted its distinction from the ciliary processes occasionally to be seen.

After the lens was removed, the equator had the appearance of frosted glass under the magnification of the preparation microscope.[28] During this early stage a few vacuoles scattered in the posterior cortex at some distance from the equator were often visible. These usually became more numerous in the following weeks and formed clusters, which often developed into a ring opacity with a garland pattern, located between the most peripheral zone and the central portion. It was composed of a great number of vacuoles of various sizes. Between this second ring opacity and the equatorial opacity the cortex was usually clear. No visible connections existed between these lenticular changes and the posterior suture. From the second ring opacity tongue-shaped extensions spread later toward the

TABLE 1.—*Onset of Cataractous Changes in Rabbit Lenses After Roentgen Irradiation with a Single Dose and with Divided Doses of 2,000 r*

Time After Irradiation	Type of Irradiation	No. of Rabbit Lenses Which Developed		
		Posterior Cortical Opacity	Anterior Cortical Opacity	Total Cataract
4-6 wk.	Single dose, 2,000 r	16	5	..
7-10 wk.	Single dose, 2,000 r	30	19	..
3-4 mo.	Single dose, 2,000 r	2	17	17*
7-11 wk.	1,000 r twice at 1 wk. interval	0	8	..
3-4 mo.	1,000 r twice at 1 wk. interval	2	..	7†
4½-7 mo.	1,000 r twice at 1 wk. interval	..	2	..
3-3½ mo.	1,000 r twice at 3 wk. interval	3	3	..‡

* Total cataract developed in five lenses between 4½ and 5½ months, and in six lenses between six and seven months, after irradiation.
† Total cataract had not developed in four lenses in four months; the eyes were not followed further clinically.
‡ Total cataract did not develop in 12 months.

posterior pole. At this time, or sometimes earlier, a mosslike, striated or net-shaped, superficial opacity became visible under the anterior capsule, usually in the upper periphery of the pupillary area.

The cataractous process advanced slowly for several weeks, but the opacity of the anterior cortex remained translucent for various lengths of time. Opaque fragments of the lens nucleus could be distinguished before the opacification of the anterior cortex progressed to the stage of full cataract, three to four months after irradiation. Pathological branching of the posterior horizontal suture, as observed by Goldmann and Liechti after roentgen irradiation of circumscribed parts of the rabbit lens, did not occur in this series. Short branches, extending upward or downward, were occasionally seen but also occurred in the nonirradiated lenses. Eyes in which the beam of radiation had been alined with the optical axis showed more corneal damage. This impaired the visibility of the early lenticular opacities,

28. This type of radiation injury to the lens must be distinguished from drying effects, which occur rapidly but can be prevented by moistening the surface of the lens.

but the general course of the developing radiation cataracts paralleled the course of the cataracts of the main series.

When 2,000 r was administered in two doses, the results varied with the length of time between sessions. Nineteen eyes were irradiated twice with an interval of one week. Here the onset of the first signs of radiation cataract was delayed an average of nine weeks. The further progress of the cataractous process was apparently slowed down, as compared with the development of lens opacities in the main series, in which 2,000 r was given in one dose. However, seven of 11 eyes observed for a sufficient length of time showed total cataract three to four months after irradiation, similar to the results obtained with the use of the undivided

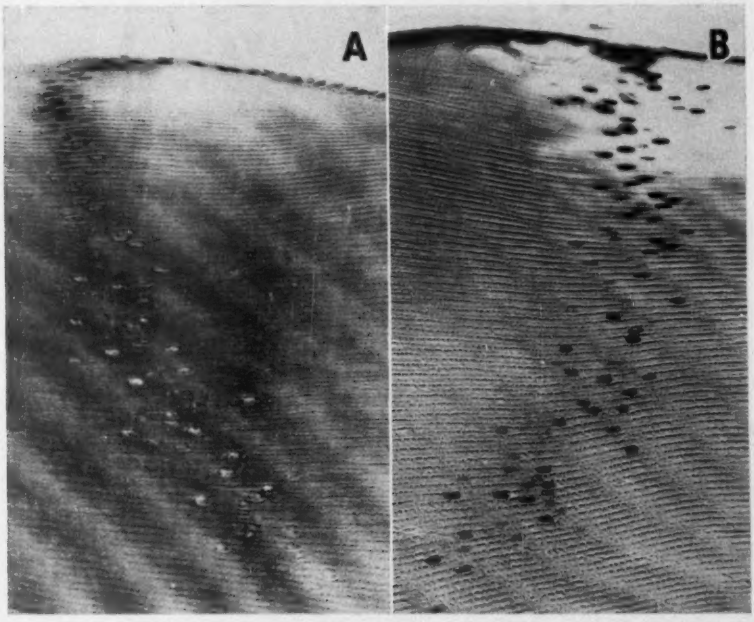

Fig. 2.—Lens bow of control eye (*A*) and of irradiated eye (*B*) with displacement of nuclei two weeks after irradiation with a single dose of 2,000 r. Hematoxylin-eosin stain; × 86.

dose. The latency period was increased to 12 weeks in a group of only four rabbits in which the two irradiations were spaced three weeks apart. The initial equatorial opacities seen at this time were followed by the development of fine lenticular changes in the posterior cortex, especially around the posterior pole, leading to a picture which resembled the roentgen ray cataract of the human eye. The opacity did not progress to a full cataract in 12 months.

Histological Observations.—The first definite deviation from the norm was a displacement backward, and sometimes forward, of some of the nuclei in the lens bow. This was noted as early as one week after irradiation. At the same time, or shortly thereafter, clumping of chromatin and karyorrhexis, with various-sized

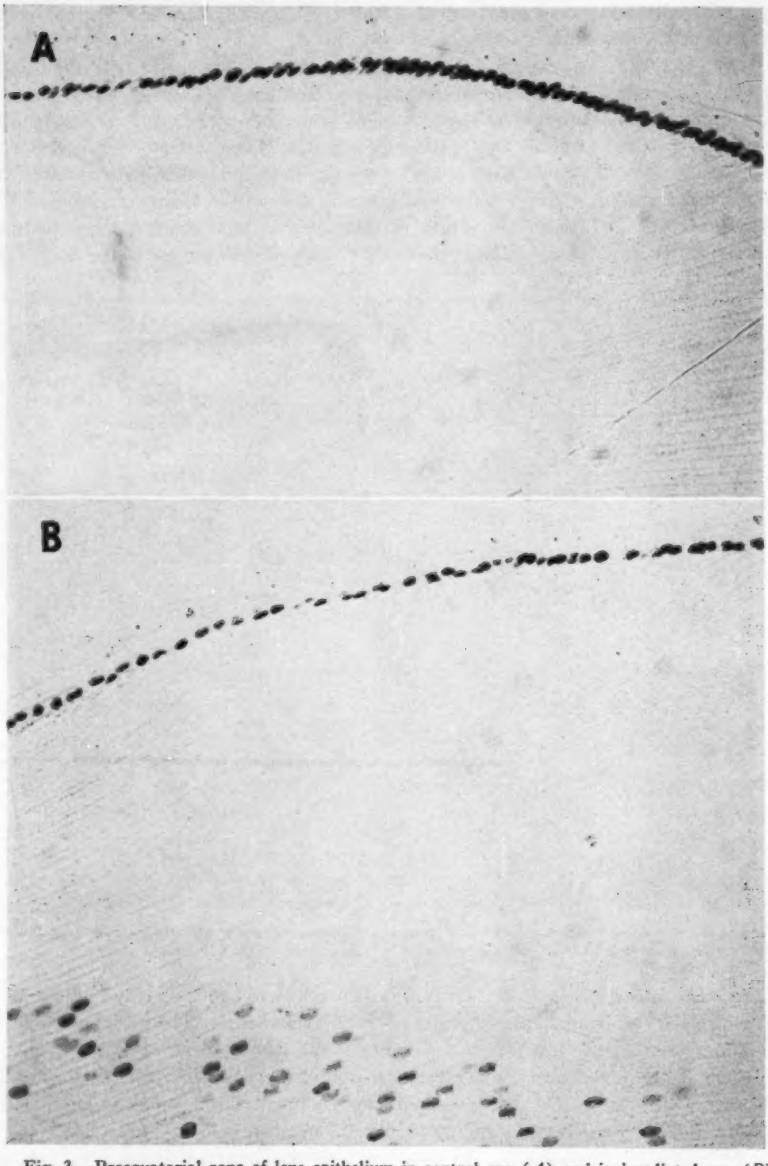

Fig. 3.—Preequatorial zone of lens epithelium in control eye (*A*) and in irradiated eye (*B*) with spatial disarrangement of nuclei four weeks after a single dose of 2,000 r. Feulgen stain; × 300.

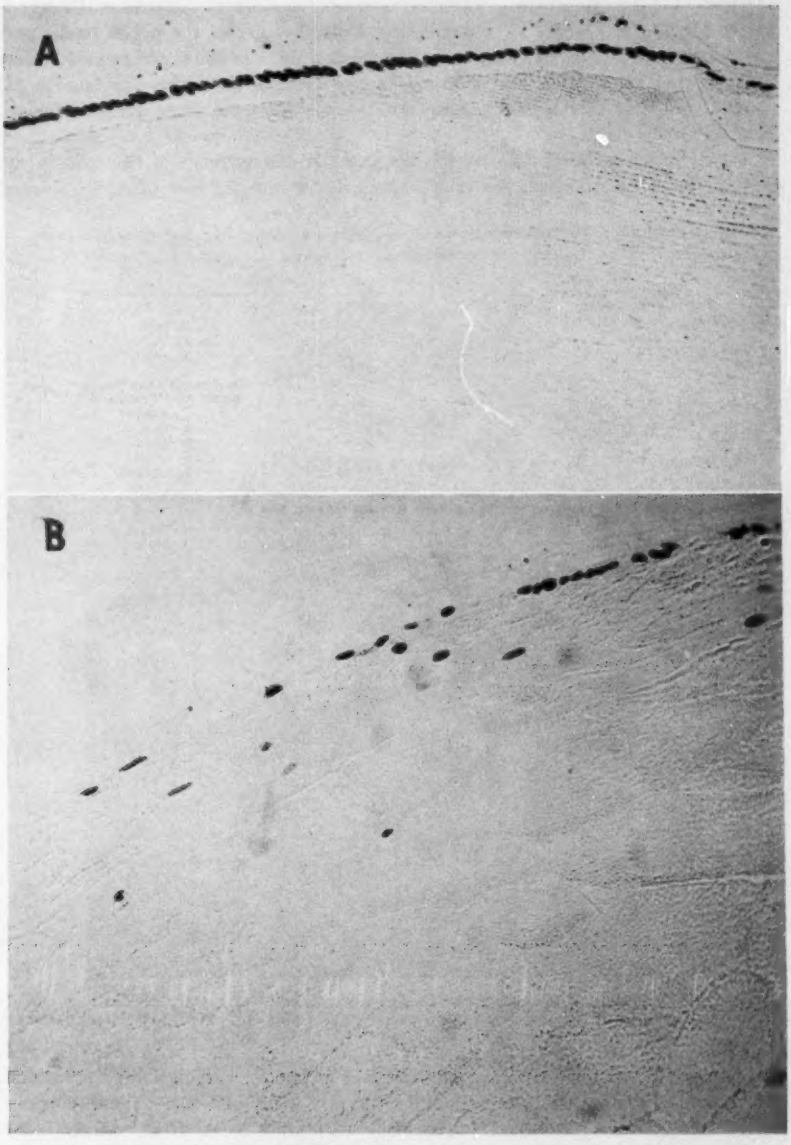

Fig. 4.—Preequatorial zone of lens epithelium in control eye (*A*) and in irradiated eye (*B*), with morphological changes and disappearance of nuclei three months after irradiation with 1,000 r twice at a three week interval. Feulgen stain; × 300.

particles of chromatin in the cytoplasm, were seen in a few of the cells of the germinative zone. Two weeks after irradiation some disorder of the nuclei in the preequatorial zone was indicated by their less regular and less dense spacing, and a few cells showed vacuolation and swelling of the cytoplasm. With the histological technic employed in this study, however, the evaluation of these earliest changes was subject to error.

After another one or two weeks, the palisade arrangement of the cells in the germinative zone vanished, the cells became flatter and the row of nuclei showed

TABLE 2.—*Cell Counts in Preequatorial Epithelium of Irradiated and Control Lenses*

Time After Irradiation, Wk.	No. of Rabbit Lenses	Counts*	
		Irradiated Eyes	Control Eyes
1	4	1. 72.66 2. 60.16	1. 99.0 2. 76.0
2	4	1. 69.3 2. 57.33	1. 91.0 2. 92.0
3	1	1. 64.2	No control; 89.5 average count for all controls
4	6	1. 56.0 2. 47.3 3. 41.0	1. 81.66 2. 91.0 3. 86.66
8	4	1. 63.0 2. 38.12	1. 85.0 2. 103.66

* Each figure is the average of counts on three sections of each lens.

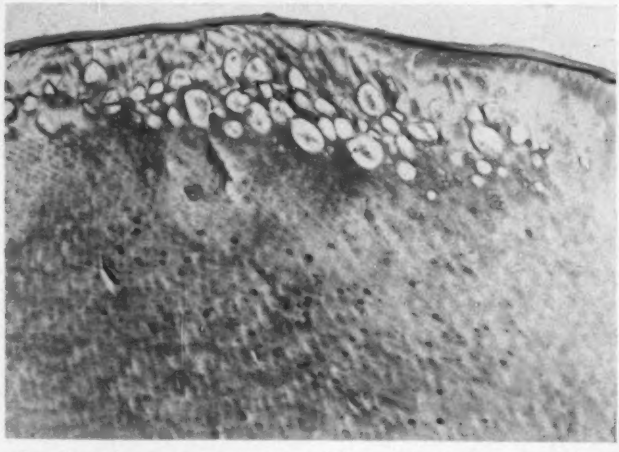

Fig. 5.—Cyst formation at subcapsular ends of fibers in front of equator of lens four weeks after irradiation with a single dose of 2,000 r (roentgen radiation.) Hematoxylin-eosin stain; × 65.

broad interruptions. Chromatin fragmentation, pyknosis, karyolysis and occasionally very large multinucleated cells could be seen in many sections. These morphological changes were reflected in the cell counts of these areas, which were significantly lower than in the control eyes. At this same time, three or four weeks after irradiation, a considerable number of nuclei from the germinative zone and from the bow had migrated backward, either subcapsularly or in the outer layers of the posterior cortex. Some of these pseudoepithelial cells showed the degenerative changes which characterize the Wedl vesicle cells.

The first differences in appearance between the lens fibers of the irradiated and those of the control eyes were noticed about three weeks after irradiation. In the irradiated eyes the fibers showed increased thickness, especially at their subcapsular endings, and a change in the angle of their insertion, which became less acute in the preequatorial and postequatorial zones. Four weeks after irradiation vacuoles, partly filled with granular matter, were observed as an excessive lesion in six lenses. They were located at the ends of fibers of medium length and formed large cystic spaces. Some of these cavities obviously arose from intrafibrillary

TABLE 3.—*Cytochemical and Morphological Changes in Paraffin Sections of Rabbit Lenses After Roentgen Irradiation with a Single Dose of 2,000 r*

No. of Lenses	Time After Irradiation	Stain Used	Stain* Intensity Exper.	Stain* Intensity Control	Stain* Irregularity Exper.	Stain* Irregularity Control	Morphological Changes
4	3 hr.	Feulgen; Methyl green†	No significant difference				.....
4	1 day	Feulgen; Methyl green	No significant difference				.....
2	3 days	Feulgen; Methyl green	No significant difference				.....
4	1 wk.	Feulgen; Methyl green	+± +±	+++ +++	+ ±	± ±	Minimal displacement of nuclei in bow
4	2 wk.	Feulgen; Methyl green	++ ++	+++ +++	+ +	± ±	Displaced nuclei in bow; atypical mitotic figures in germinal zone
2	3 wk.	Feulgen; Methyl green	++ ++	+++ +++	+ +	± ±	Marked displacement of nuclei in bow; cell arrangement irregular—fewer cells, wider spread in germinal zone
6	4 wk.	Feulgen; Methyl green	++ ++	+++ +++	++ ++	± ±	Few nuclei in germinal zone; nuclei pyknotic and hyperchromatic; palisade arrangement lost; cells flat at germinal zone; lens fibers swollen, irregular and with cystic spaces in germinal zone
4	8 wk.	Feulgen; Methyl green	+ +	+++ +++	+++ +++	± ±	Broad interruptions in germinal zone; extensive degenerative changes in nuclei; scarcity of cells in bow; lens fibers greatly swollen, irregular and with cystic spaces

* Intensity and irregularity are graded by arbitrary plus (+) signs.
Normal intensity is indicated as +++; slightly less than normal, as ++±; less, as ++, and much less, as +.
Marked irregularity is shown as +++; moderate irregularity, as ++; slight irregularity, as +, and very slight irregularity, as ±.
† Methyl green staining was evaluated approximately in milligrams per 100 cc. of desoxyribonucleic acid, +++ being approximately 800 mg. per 100 cc., ++ approximately 200 to 400 mg. per 100 cc. and + approximately 100 mg. per 100 cc.

vacuoles; others may have developed from interfibrillary clefts. This system of cysts formed complete rings from 1 to 2 mm. in front of and behind the equator. Clinical examination of the same lenses by transillumination had revealed brilliantly reflecting vacuoles located either at the lateral ends of the posterior horizontal suture or along its entire length. Microscopic examination of the posterior calottes of these preparations confirmed the location of the large vacuoles at the ends of the long fibers, i. e., at a maximal distance from the equator. These vacuoles disappeared in a few weeks without residue in the two eyes, which were not removed for histological examination. Histologically, the severity of the radiation damage at the subcapsular ends of the fibers contrasted with the moderate degree of the changes in the nuclei of the preequatorial zone and of the bow.

Comment.—The early ophthalmoscopic signs of experimental roentgen ray cataract observed in this study resembled those observed by Leinfelder and Kerr. These investigators first noted bubbles at the periphery of the lens, which later covered most of the posterior subcapsular region. The early histological changes in the lens epithelium after roentgen irradiation in the present series were similar to those observed by Poppe in rabbits, although in the main he used a different histological method. In both studies the radiation factors were in the same range of magnitude. Okusawa also described degenerative changes in the nuclei of the lens epithelium of rabbits before opacities formed. There is no doubt that the injurious effects caused by this type and dose of radiation first became visible microscopically in the nuclei of the epithelial cells in the germinative zone and, in our experiments, in the nuclei of the bow. These effects could be observed about seven days after irradiation. Poppe was able to identify signs of abnormal cellular division on the sixth day. The technic used in the present study did not lend itself to investigation of changes in mitotic activity caused by roentgen radiation or to an analysis of the timing of effects on mitosis. It might be concluded from the studies of Poppe that the response of the lens epithelium to exposure to roentgen rays resembled that of other types of epithelium which have been studied more extensively.

Very slight differences of thickness and of direction of growth of the lens fibers were observed in a few instances two weeks after exposure to roentgen rays. These changes could be recognized only by comparing the sections of the experimental lenses with those of the control lenses which had been treated histologically in exactly the same way and were mounted on the same slide. The microscopic signs of radiation injury were in evidence, therefore, from two to four weeks before the ophthalmoscopic examination of the equatorial area revealed the first opacity in the form of a fine, dark ring. These opacities were apparently caused by rather advanced destructive processes of the youngest peripheral lens fibers, with the formation of vacuoles and swelling of the fibers as the most important microscopic substrate. Although the migration of nuclei backward, under or near the posterior lens capsule, was conspicuous at this stage, there was no indication that the development of the pseudoepithelial cells and Wedl vesicle cells had anything to do with clinically visible opacities at the equator or in the superficial layers of the posterior cortex, as was suggested by Aulamo.

It could not be concluded from the results of this study that the lesions of the nuclei, which preceded those of the fibers, were necessarily the cause of the decomposition of the fibers at their ends. The excessive formation of large cystic spaces at this location, and in part at a great distance from the nuclei, as observed in six eyes four weeks after irradiation, rather indicated a direct injury to the cytoplasm. The well known degenerative changes of the nuclei of the epithelium in these eyes did not exceed those in other irradiated eyes in which the fibers were changed but to a very slight degree. Young lens fibers and their nuclei are considered as a nutritional unit, and the possibility could therefore not be excluded that the severe damage of the cytoplasm had been detrimental to the nucleus in these instances.

Cytochemical Changes

The cytochemical effects of ionizing radiations in their biologic actions are the subject of far reaching radiobiological research. In summing up the recent

literature, one might say that according to many workers a change of chemical nature is an early event in the chain of reactions. Zirkle [29] remarked that biologic structures are built by chemical means, so that one can "hardly imagine a morphological change which does not involve chemical changes." The proponent of the hypothesis that disturbance in the chemistry of the cells invokes structural signs of radiation injury is confronted with the difficulty of explaining the disproportion between the low magnitude of the chemical change and the prominence of the biologic action. Various explanations have been offered to overcome this theoretical objection.

In general, it is assumed that for many biologic responses the irradiation of the cell nucleus is more consequential than the irradiation of the cytoplasm. The most important chemical constituent of the cell nucleus is desoxyribonucleic acid. For this reason, and in view of the reports by Ahlström, von Euler and Hevesy [30] and Stowell [31] on the blocking of the formation of desoxyribonucleic acid in tissue by roentgen rays, a first attempt was made in this study to observe by cytochemical methods changes of this acid in amount and polymerization in the nuclei, and of ribonucleic acid in the cytoplasm, of the lens after irradiation. The technics employed have already been described. The possibility of comparing directly in the same areas of paraffin sections the staining intensities in experimental and in control lenses permitted certain conclusions to be drawn, in spite of the fact that quantitative methods of great accuracy could not be employed.

Material.—Fifteen pairs of lens preparations were submitted to the cytochemical reactions on paraffin sections with time lapses of from three hours to eight weeks after irradiation. Flat preparations of lens epithelium served for quantitations of desoxyribonucleic acid in 12 instances (seven irradiated, and five control lenses). Irradiated and control eyes were used, as well as eyes of nonirradiated animals of the same age group, in view of the possible effect of indirect irradiation on the control lenses. In this group the experiments were terminated one hour, three hours, one day and three days after irradiation. The indirect radiation effect on the second eye, shielded and outside the beam, was determined in three experiments by placing an ionization chamber in the orbit of this side during the exposure of the other eye to 2,000 r.

Observations.—The orbit on the shielded side received 7 r, i. e., 0.33 per cent of the radiation employed directly on the other eye. Nuclei of the epithelium in normal and in control lenses stained well in flat preparations, both with the Feulgen technic and with methyl green. The nuclei of the germinative zone showed deeper staining than the nuclei of the anterior surface. Similar results were obtained on the lens epithelium in paraffin sections when Stowell's modification of the Feulgen reaction was followed closely in all steps. The nuclei of the lens bow took the color poorly. Methyl green stained the nuclei of the germinative zone more brilliantly than the nuclei of other epithelial cells of the lens. The nuclei of the bow were

29. Zirkle, R. E.: Relationships Between Chemical and Biological Effects of Ionizing Radiations, Radiology **52**:846, 1949.

30. Ahlström, L.; von Euler, H., and Hevesy, G.: Über die kurzlebige durch Röntgenstrahlen bewirkte Hemmung der Nukleinsäurebildung, Ark. Kemi Mineral. Geol. 1944, vol. B18, no. 13; Die Wirkung von Röntgenstrahlen auf den Nukleinsäureumsatz in den Organen der Ratte, ibid., 1945, vol. A19, no. 9; von Euler, H., and Hevesy, G.: Wirkung der Röntgenstrahlen auf den Umsatz der Nukleinsäure in Jensen-Sarcom II, ibid., 1944, vol. A17, no. 30.

31. Stowell, R. E.: Effects of Roentgen Radiation on Thymonucleic Acid Content of Transplantable Mammary Carcinomas, Cancer Research **5**:169, 1945.

often almost colorless. These observations indicate that there is a greater content of desoxyribonucleic acid of a high degree of polymerization in the preequatorial area than in other areas. Despite the purification and repeated recrystallization of pyronin, there existed gross inhomogeneities in the intensity of staining with this dye, even in individual sections, and the results could therefore not be evaluated.

At the stated intervals, i. e., one hour up to three days after irradiation, no difference in staining intensities of the nuclei could be demonstrated between experimental and control eyes in flat preparation of lens epithelium. Lenses from nonirradiated animals were found not to be suited for comparisons because of individual biologic variations. The amount of desoxyribonucleic acid of many nuclei in the preequatorial zone, as shown with the Feulgen reaction in paraffin sections, appeared diminished two to three weeks after irradiation. There was also less intense staining with methyl green in approximately the same number of nuclei in this area. The examination conveyed the impression of a decrease in the highly polymerized form of the acid in these individual cells. Other nuclei did not differ in their color from those in the control lenses, and some nuclei were stained more deeply than average both with the Feulgen and with the methyl green technic; they then usually showed chromatin clumping or advanced pyknosis. In later stages, beginning four weeks after irradiation, the differences in the staining characteristics between the two sets of sections were more pronounced, but signs of nuclear degeneration were then also more conspicuous. In the earlier phase it could not be shown convincingly with the technic used that the pale-staining nuclei were free of structural changes. Variations in the staining similar to those in the germinative zone were seen to a much slighter degree on the surface epithelium and were not visible in the cells of the bow. However, meridional sections limited the possibilities of examining the flat cells of the surface epithelium under favorable conditions.

Comment.—Ahlström, von Euler and Hevesy used radioactive phosphate as an indicator in their studies on the effects of roentgen radiation on the turn-over of desoxyribonucleic acid and concluded that the amount of the newly formed desoxyribonucleic acid in the course of two hours was reduced by preceding roentgen irradiation to one-half or one-third its normal value. Similar influence of radiation on the turn-over of this chemical constituent of the cell nucleus was noted in the Jensen sarcoma and in normal organs of rapidly growing or adult rats. The reduction in the formation of labeled nucleic acid in the irradiated sarcoma was only 25 per cent less than that in a second shielded sarcoma on the other side of the animal. Radiation measurement in the shielded sarcoma gave a reading of only a few roentgen. Stowell determined the content of desoxyribonucleic acid of transplanted mammary carcinoma in rats and mice by means of the Feulgen reaction and a photomicrometric technic. The tumors on one flank of the animal were irradiated, and those on the other side were protected with lead shielding. Stowell did not report on measurements of secondary and back-scatter radiations on the protected side. The directly irradiated tumors presented a mean decrease of 13 per cent in desoxyribonucleic acid per area in rats and of 5 per cent in mice. According to Stowell, his results "support a hypothesis that roentgen radiation may alter the molecular structure of vital substances within the nucleus and produce a disturbance of the nucleoproteins, which in some instances is followed by death of the cell." The decrease in desoxyribonucleic acid in radiated

cells would suggest "that one of the most important intracellular effects of roentgen radiation is the production of an upset in the normal balance and metabolism of both types of nucleic acids." In earlier experiments Mitchell [32] demonstrated an increase of ribonucleotides in the cytoplasm of irradiated cells.

In the present study an attempt was made to observe differences in content of desoxyribonucleic acid and ribonucleic acid in nuclei and fibers of the lens irradiated with 2,000 r (roentgen radiation) and the content in shielded (control) eyes which were exposed to indirect irradiation with 7 r. The results of the specific staining procedures for these acids in the series should be considered preliminary, since they were not based on accurate quantitative methods. The deviations in staining intensities were verified, however, by the independent observations of two or three workers. Their estimation suggested that desoxyribonucleic acid was reduced in amount and polymerization in individual cell nuclei of the germinative zone about two weeks after irradiation. Later many nuclei showed a greatly decreased Feulgen reaction and a pale-staining response with methyl green. Pyknotic nuclei stood out by their intense color. The decrease in highly polymerized desoxyribonucleic acid, as shown with the methyl green, paralleled the change in the Feulgen reaction. The irregularities of the staining properties of pyronin did not permit any conclusions as to the content of ribonucleic acid in the cytoplasm.

Although the decrease of desoxyribonucleic acid in the germinative zone of the epithelium seemed to accompany degenerative changes in the nuclei, rather than precede them, no definite statement could be made on the sequence of a decrease in staining and structural alterations. Finally, it should be stressed that all results reported here were obtained with one technic of roentgen irradiation and are not to be compared with the results of experiments in which very different irradiation technics were employed.

SUMMARY

1. Cataractous changes became demonstrable with the ophthalmoscope in 53 of 56 rabbit eyes four to 10 weeks after they had been irradiated with 2,000 r of penetrating roentgen rays. The opacities started at the equator of the lens and progressed in the posterior cortex, and then in the anterior cortex, in characteristic patterns.

2. Acute exposure of rabbit eyes to a dose of 2,000 r of penetrating roentgen rays was followed histologically as early as one week after irradiation by spatial disarrangement and initial morphological changes of the nuclei in the bow and in the preequatorial zone of the lens epithelium. In the second and third weeks degenerative changes of the nuclei in this area became more pronounced, with a considerable decrease in the number of these tissue elements and with gaps in the epithelial row of the preequatorial zone.

3. Swelling and disorganization of lens fibers were usually observed after changes in the cell nuclei had advanced, but in six of the 56 irradiated eyes of the series extensive cystic formations at the subcapsular ends of the lens fibers four weeks after irradiation suggested a direct radiation effect on the cytoplasm.

32. Mitchell, J. S.: Disturbance of Nucleic Acid Metabolism Produced by Therapeutic Doses of X and Gamma Radiations: III. Inhibition of Synthesis of Thymonucleic Acid by Radiation, Brit. J. Exper. Path. **23**:309, 1942.

4. The content of desoxyribonucleic acid in nuclei of normal lens epithelium could be well demonstrated by the Feulgen technic, and the highly polymerized form of the acid could be shown with methyl green. The nuclei of the germinative zone appeared especially rich in this constituent. Staining for ribonucleic acid in the cytoplasm with pyronin did not give reliable results.

5. The cytochemical studies indicated that two weeks after irradiation individual nuclei in a given area contained less desoxyribonucleic acid of high polymerization than nuclei in a comparable area of the control lens, but it was not clear whether or not the staining differences preceded the structural signs of nuclear degeneration.

CORNEAL ULCER PRODUCED BY AEROBACTER AEROGENES

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OCULAR infections due to Aerobacter aerogenes have not been reported so far as can be determined. In 3,630 preoperative cataract cultures, A. aerogenes has been found only once.[1] However, 10 cases of chronic conjunctivitis due to A. aerogenes have been encountered in this laboratory in the last 10 years. The strains tested have proved sensitive to streptomycin. This organism is widely distributed in nature,[2] being found in the soil, in feces, in water and in milk. Besides being present in the upper regions of the intestinal canal, it may cause infections of the urinary tract in man. A. aerogenes is a gram-negative, non-spore-forming, frequently encapsulated bacillus, which may be motile or nonmotile. It is a facultative anaerobe, being readily cultivated on all ordinary mediums, and it ferments a great variety of carbohydrates.[2]

REPORT OF A CASE

H. R., a man aged 31, was first seen in the outpatient clinic because of bilateral congenital ptosis. Examination showed total absence of levator action on both sides, and a Motais procedure was carried out on the right eyelid, with an uneventful postoperative course and satisfactory cosmetic and functional results.

Three weeks after the first operation a similar procedure was carried out on the left upper lid. On the fourth postoperative day the patient complained of irritation, and when the dressing was removed, it was found that, with the postoperative swelling and the restriction of the Frost suture, an entropion had occurred, with abrasion of the cornea. All sutures were removed, and the conjunctival sac was filled with penicillin ointment (1,000 units per cubic centimeter). On the following day the entropion persisted, and intermarginal sutures were placed to hold the lid margins in place. These sutures were removed two days later, and the upper half of the cornea was found to be diffusely infiltrated. Penicillin ointment was instilled into the conjunctival sac, and the intermarginal sutures were replaced. This procedure was repeated in four days, with little change in the appearance, but inspection of the cornea after

From the Departments of Ophthalmology and Bacteriology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of the Presbyterian Hospital.

1. Dunnington, J. H., and Locatcher-Khorazo, D.: Value of Cultures Before Operation for Cataract, Arch. Ophth. **34**:215 (Sept.) 1945. Khorazo, D., and Thompson, R.: The Bacterial Flora of the Normal Conjunctiva, Am. J. Ophth. **18**:1114, 1935.

2. Dubos, René J.: Bacterial and Mycotic Infections of Man, Philadelphia, J. B. Lippincott Company, 1948. Jordan, E. O., and Burrows, W.: Textbook of Bacteriology, ed. 14, Philadelphia, W. B. Saunders Company, 1946.

another four days revealed ulceration centrally and a small hypopyon. Cultures were taken, and the patient was placed under treatment with penicillin and aureomycin, administered systemically. Penicillin also was given locally in the form of drops every hour and injected subconjunctivally three times a day. The cultures showed a gram-negative organism, which proved to be A. aerogenes.

The ulcerated area extended across the center of the cornea, with ragged edges and a gray, thin base. The hypopyon remained in a gelatinous clump under the temporal half of the ulcer (rather than leveling off in the lower angle of the anterior chamber), and the edge and base of the ulcer were dirtier in this portion.

There was little change during the next five days, and a keratotomy was done, with the primary intent to wash out the anterior chamber. Streptomycin, to which the organism had been proved to be sensitive, was substituted for the penicillin in subconjunctival injection. After this there was a striking remission in symptoms, and the hypopyon did not reform for three days, at which time the section and irrigation with saline solution were repeated. This procedure was again carried out three days later, subconjunctival injection of streptomycin being continued daily. Two days after this a definite subjective and objective improvement was noted; cultures became sterile for the first time, and the entire process came to a stop in the next 12 days and went on to complete healing, with a dense, white central leukoma, which reduced vision to finger counting.

The total course of the infection was 28 days, in 23 of which the patient was under treatment with streptomycin, to which the organism was sensitive.

General supportive measures, instillation of atropine and local application of heat were carried out during the course of the disease.

Laboratory Findings.—Dec. 24, 1948: Bacteriologic studies[3] were made after the patient's second admission. Cultures of the conjunctiva of the normal (right) eye revealed nonpathogenic Staphylococcus albus and diphtheroids. The lid had, in addition to the nonpathogenic Staph. albus, 14 colonies of a gram-negative bacillus.

Left Eye: Cultures of the conjunctiva and lid yielded numerous colonies of gram-negative bacilli and a few colonies of nonpathogenic Staph. albus. Direct smears from the conjunctiva of this eye revealed numerous polymorphonuclear cells, a few gram-negative bacilli and an occasional gram-positive Diplococcus. Scrapings from the conjunctiva stained by the Giemsa method showed numerous polymorphonuclear cells and moderate numbers of lymphocytes, but no organisms were seen.

December 27: The conjunctiva of both eyes revealed numerous gram-negative bacilli. In addition the gram-negative bacilli were found in a culture from the cornea. From the nose, throat, stool and urine a gram-negative organism was also isolated on culture which morphologically resembled closely the gram-negative bacilli found in the eyes. This gram-negative bacillus, isolated from the conjunctivas and the lids, nose, throat, urine and stool, was a nonmotile, non-acid-fast and non-spore-forming organism. It was identified as A. aerogenes on the basis of morphological and cultural characteristics and of the standard biochemical tests. Further bacteriologic examinations of the eyes after treatment did not reveal the presence of the organism.

Sensitivity to Antibiotics: By standard in vitro methods, the A. aerogenes proved to be resistant to penicillin and aureomycin but sensitive to streptomycin.

Pathogenicity for Animals: Adult white mice: Death within 18 to 24 hours followed the intraperitoneal injection of 0.1 cc. of an 18 hour culture of the organism. A. aerogenes was recovered at autopsy. The same results were obtained when the mice were given injections of the organism isolated from the urine, stool, nose and throat.

Guinea Pigs: Intraperitoneal injections of 0.2 to 1 cc. of the 18 hour culture had no effect. The organism isolated from the nose, throat, stool and urine inoculated in the same way as in the mice also proved nonvirulent for the guinea pigs.

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3. Mrs. Elizabeth de Montmollin gave technical assistance.

Rabbit: A dose of 0.03 cc. of an 18 hour culture of the A. aerogenes injected into the anterior chamber of a rabbit eye produced exudative iritis. A similar condition was noted with the injection of a sterile filtrate of the A. aerogenes.

SUMMARY

1. Aerobacter aerogenes was isolated in a case of corneal ulcer. The same organism was found also in the nose, throat, stool and urine of the patient.

2. All the isolated strains of A. aerogenes proved to be sensitive to streptomycin, which was used therapeutically with success.

3. The strains of A. aerogenes were nonpathogenic for guinea pigs but produced a fatal infection in mice. One strain from the eye induced exudative iritis when injected into the anterior chamber of a rabbit's eye.

PRELIMINARY NOTE ON STUDY OF THE REFRACTIVE STATE, WITH SPECIAL REFERENCE TO MYOPIA

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THE INQUIRY into the state of refraction of an "advanced community" in the Deccan, which is a fairly homogeneous group, was undertaken under the auspices of the Indian Council of Medical Research. The ages of the first group of subjects were between 6 and 12 years. The data are based on the examination of a sample of 590 unselected school children, which may be taken to represent the refractive state of the community before important environmental factors came into operation. In the same investigation, the heights, weights and blood pictures of the children, whenever possible, were recorded.

The frequency curve plotted for this series shows the mean refraction to be + 1.0 D., the mode + 1.25 D. and the standard deviation + 1.0 D. The curve for variation of refraction according to age indicates a definite downward trend, the average refraction at the age of 7 years being + 1.5 D., whereas at the age of 13 it is + 0.5 D. A study of the relation of refraction to height indicates that, for a given age, higher refractions are associated with shorter heights. The coefficient of partial correlation between refraction and height when age is eliminated is found to be —0.3. There is unmistakable evidence that subjects with subnormal heights have higher (more hypermetropic) refractions, while subjects who are taller for their ages have lower (less hypermetropic) refractions. It is interesting to note that in a small series of subjects with pathological myopia the same observation could be established. Thus, the heights of these myopes are greater than the average for their ages. The actual weights of such persons are lower than average for their ages. The blood pictures appear to show a significant difference in the values for serum calcium between the pathological subjects and others. The study of this aspect in a later age group of the same community is in progress.

It appears from the data thus far collected that the state of refraction is determined mainly by factors concerned with body growth and that the factor of nutrition is of secondary importance in the development of pathological myopia. It will be interesting to study how far the growth hormones of the pituitary gland, which are known to regulate the development of the body skeleton, play any part in this process.

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DEVELOPMENT OF ELECTRO-OCULOGRAPHY

Standing Potential of the Eye in Registration of Eye Movement

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EYE MOVEMENTS[1] are an important physiological activity. For many purposes it is no longer sufficient to observe gross eye movements subjectively. Instruments must be used which can measure objectively eye movements over a large range and to a small angle, follow rapid changes for long stretches of time and be used under a variety of experimental and clinical situations.

There are three fundamental methods by which eye movements can be objectively recorded (Duke-Elder[2]). The first is by a mechanical (or hydraulic) system attached directly to the eyeball. This crude method has been completely supplanted by the other two.

The optical method of recording rotations of the eyes is better known. Reflections from the cornea—the first Purkinje image—of a light source is recorded photographically on a moving film. There are several disadvantages to this procedure. The head is immobilized, and generally a strong glare comes from the light source. The eyes must be kept open; even blinking may spoil an important part of the record. A complicated optical system is necessary if registration is to be made in two instead of one meridian. Furthermore, it is time consuming to await photographic development of the film.

The third method of registering eye movements—the electrical method—has none of these disadvantages. Its accuracy and precision, however, are open to question.

This review discusses corneoretinal potentials generally and electro-oculography critically. Further, it mentions possible applications of the electro-oculogram and makes suggestions for future research.

ELECTRODES AND INSTRUMENTS

In order to pick up electric currents from tissue, it is necessary to have a metal-nonmetal junction somewhere in the circuit. The metal may be applied either directly to the tissue or indirectly through a special coating—paste, jelly or solution. The metal, and its coating, used to pick up electric currents from tissue is called an electrode. Sometimes the term electrode is

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1. By eye movements are meant here nystagmus and those normal rotatory movements of the eyeball which are voluntary or a response to light stimuli. They are generally not much smaller than 15 minutes of arc. Involuntary micro-ocular movements, often called physiological nystagmus, are not considered in this review.

2. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 1, pp. 585-587.

used to designate all the components when made up into a single unit, usually in a glass container, e. g., the metal and its coating, the wick, which comes in contact with the tissue, and the saline solution, which bathes all of the components.

The choice of an electrode is important. It usually is not given the attention it deserves. It is sufficient to say here that the phenomenon of electrode polarization may cause serious errors when used with certain types of currents and measuring instruments. Hence, electrodes which minimize polarization are generally desired and are called nonpolarizable electrodes.

Platinized platinum and silver-silver chloride electrodes show relatively little polarization. Polarization, moreover, is a function of the current density, so that the area of the electrode is important.

Ideally, no power should be drawn from the tissues in measuring bioelectricity. The best practical solution, however, in the measurement of corneoretinal potentials lies in the direct current vacuum tube amplifier with a high impedance input. Thus, the current drain is at a minimum, and variations of current of long duration are unmistakably recorded. The amplifier may be fed into a cathode ray oscilloscope for careful investigation. For clinical work, an ink-writer oscillograph gives an inexpensive and immediate written record.

The topic of bioelectricity, electrodes and instrumentation will be more fully covered elsewhere (Marg [3]).

CORNEORETINAL POTENTIALS

When an electrode is placed on the cornea of an animal in the dark and another is placed near the posterior pole of the eye or elsewhere on the head or body a potential may be found. It is called by any of the following names:

Steady Static Standing	} potential	(*Bestandstrom*)
Dark potential		(*Dunkelstrom*)
Resting potential		(*Ruhestrom*)

This potential is of the order of 1 millivolt when taken indirectly on human beings.

Credit for the discovery of the standing potential is generally given to du Bois-Reymond [4] (1849). Here, in his own (translated) words, is the announcement of his discovery in the tench, a European freshwater fish.

> . . . With the eye on its side, the cornea and optic nerve could be brought into contact with the electrodes. From this it was shown that an arbitrary point of the surface of the eyeball was positive relative to the cross section of the optic nerve.

From this, one can only conjecture whether du Bois-Reymond knew whether he was getting the physiological standing potential or the current of injury (demarcation current) from the cut end of the optic nerve. He was, no doubt, getting both simultaneously.

If while the electrodes are still in position for the resting potential the eye is illuminated, there occurs a multiphasic potential, variously called illumination potential (*Belichtungstrom*), action potential (*Aktionsstrom*) and photoelectric potential (*photoelektrischer Strom*). This potential gives a record which is called the electroretinogram (*Elektroretinogramm*). It occurs as an addition to the standing potential. A review of the electroretinographic literature may be found in Granit [5] (1947).

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3. Marg, E.: To be published.

4. du Bois-Reymond, E.: Untersuchungen über thierische Electricität, Berlin, G. Reimer, 1849, vol. 2-1, p. 256.

5. Granit, R.: Sensory Mechanisms of the Retina, with an Appendix on Electroretinography, London, Oxford University Press, 1947.

Electrical stimulation of, and mechanical insults or injury to, the eye, which may be unavoidable, give rise to blaze potentials (*Flammströme*), or currents of injury (*Verletzungsströme*). They are considered artefacts and hardly deserve classification under corneoretinal potentials.

The terminology in some of the American literature has been confused by the use of "corneo-retinal potential," in lieu of "standing potential" or one of its synonyms (Mowrer, Ruch and Miller[6]; Fenn, Galambos, Otis and Rahn.[7]) It is more reasonable to use "corneoretinal potential" for *all* potentials with the topographic distribution described. The two major subdivisions under the corneoretinal potential are, then, the standing potential and the illumination potential.

Kohlrausch[8] (1931) thoroughly reviewed the literature on corneoretinal potentials. In summarizing, he brought out several interesting points concerning the nature of this phenomenon. Since discussions of these features are not all available in English, it may be well to mention them here.

1. In vertebrates the cornea is positive relative to the retina. In invertebrates, however, the anterior of the eye is negative. This corresponds to the difference in orientation of the retinas of subphylum Vertebrata and the retinas of the invertebrates, the visual cells pointing outward in the former and inward in the latter.

2. The polarity of the standing potential is increased by light (the illumination potential) whether the animal has a positive cornea (vertebrate) or not (invertebrate).

3. There is a sudden discontinuity in potential at the ora serrata, which is found as one measures the topographic distribution of voltage.

4. Under certain influences, such as ionic changes or mechanical insults, there are independent changes of the standing and the illumination potential.

5. One finds a similar alteration in both the standing and the illumination potential under other influences, such as changes in carbon dioxide, and oxygen tensions, temperature and electrical stimuli.

It would appear that the evidence is strong in favor of the retina as the site of origin of the corneoretinal potentials. On the other hand, evidence for a Donnan membrane equilibrium potential at the blood-aqueous barrier as the origin of the standing potential seems correspondingly poor (Schaefer[9]). In fact, the retina may be thought of as a combination of a selenium photoelectric cell and a battery in series where there is a constant electric current (standing potential) which increases with irradiation (illumination potential).

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6. Mowrer, O. H.; Ruch, T. C., and Miller, N. E.: The Corneo-Retinal Potential Differences as the Basis of the Galvanometric Method of Recording Eye Movements; abstracted in Psychol. Bull. **32**:566-567, 1935.

7. Fenn, W. O.; Galambos, R.; Otis, A. B., and Rahn, H.: Corneo-Retinal Potential in Anoxia and Acapnia, J. Applied Physiol. **1**:710-716, 1949.

8. Kohlrausch, A.: Elektrische Erscheinungen der Augen, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Springer-Verlag, 1931, vol. 12, pt. 2, pp. 1393-1496.

9. Schaefer, H.: Elektrophysiologie: Spezielle Elektrophysiologie, Vienna, Franz Deuticke, 1942, vol. 2, p. 199; Ann Arbor, Mich., J. W. Edwards, 1944.

Recent work on the frog tends to confirm the concept of a very close relationship of the corneoretinal potentials (Wulff and Freyburger [10]). In human beings, the standing potential is not a reliable measure of acapnia or anoxia (Fenn, Galambos, Otis and Rahn [7]).

THE ELECTRO-OCULOGRAM

Registration of Eye Movement by Means of the Standing Potential.—The standing potential, although originating in the eye, is not limited to it but spreads outward into the adjacent tissues. If electrodes are placed just nasal and temporal to the palpebral fissure, each electrode is approximately equidistant from the positive corneal pole and the negative posterior pole of the eye. The net effect, assuming that the surrounding tissues conduct uniformly, is that no potential from the eye is measured.

If the eye should be turned inward, say as far as it can go, the nasal electrode will be much nearer the positive corneal pole than the negative posterior pole. On the other hand, the temporal electrode will be much nearer the negative posterior pole than the positive corneal pole. Hence, the nasal electrode will be positive and the temporal electrode negative. One can see, therefore, that the greater the angle of lateral rotation of the eye from its straight-ahead, "zero" position, the greater will be the component of the standing potential which is picked up. In short, the sign of the potential gives the direction of rotation; the degree of potential gives the degree of rotation.

It might be helpful to mention at this point that the eye is somewhat analogous to a rotatable battery situated within a conducting medium. The problem of recording is essentially different from that confronting the electrical engineer, who ordinarily deals with currents flowing through linear conductors, i. e., wires. The current from the eye flows in an infinite number of paths through the orbit and head; but, all things being equal, the closer to the eye, the stronger the potential. In electrocardiography one does find linear propagation, but only in the limbs (Johnston [11]).

With given electrodes and the eye fixed, the size of the observed potential depends, to some degree, on the passive electrical characteristics of the surrounding tissue, in addition to the activities of the cells in which the potential originates.

HISTORY AND DEVELOPMENT OF THE ELECTRO-OCULOGRAM

Almost 75 years ago Dewar and McKendrick [12] (1873) had begun to experiment with the electroretinogram of animals. A few years later Dewar [13] (1877) reported his observations on the human eye. He used a small trough of clay or paraffin constructed around the margin of the orbit holding dilute sodium chloride solution:

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10. Wulff, V. J., and Freyburger, S. W.: Relation Between Resting and Action Potential in the Frog Eye, abstracted, Anat. Rec. **101**:665, 1948.

11. Johnston, F. D.: Electrocardiography, in Glasser, O.: Medical Physics, Chicago, The Year Book Publishers, Inc., 1944, vol. 1, pp. 352-361.

12. Dewar, J., and McKendrick, J. G.: On the Physiological Action of Light: I and II., J. Anat. & Physiol. **7**:273-281, 1873; Recent Researches on the Physiological Action of Light, Nature, London **8**:204-205, 1873. (Article actually unsigned and written in third person.)

13. Dewar, J.: The Physiological Action of Light, Nature, London **15**:433-435, 1877.

Into this solution the terminal of a non-polarizable electrode was introduced, and in order to complete the circuit the other electrode was connected to a large gutta-percha trough containing salt solution into which one of the hands was inserted. By a laborious process of education it is possible to diminish largely the electrical variation due to involuntary movements of the eye-ball and by fixing the eye on one point with concentrated attention, another observer, watching the galvanometer, and altering the intensity of the light can detect an electrical variation similar to what is seen in other animals. This method, however, is too exhausting and uncertain to permit of quantitative observations being made.

Obviously, Dewar realized that eye movement could give changes in potential, but for his experiment these changes were merely artefacts rather than phenomena of interest to be investigated.

It was almost a half-century later before Schott[14] (1922), not knowing of Dewar's findings, looked for a more flexible method of recording eye movement than direct mechanical or photographic technics. He had some strange notions about the origin of the potential he found.

. . . In the eye it is not a question of biological currents or of electro-osmotic phenomena, but purely one of mechanical phenomena.

His two electrodes were of copper wire 0.4 to 0.5 mm. thick and mounted, one nasally and one temporally, on the left side of a horn rim eyeglass frame. The wires were then spiraled into the form of a spring. The one on the nasal side ended in a spherical button 2 mm. thick of polished copper and rested on the caruncle of the cocainized eye. On the temporal side the wire end was bent back into a loop 2 to 3 mm. in diameter, which rested on the bulbar conjunctiva in the outer canthus. These electrodes were wired directly to a string galvanometer of an electrocardiograph. Schott's primary interest was nystagmus, as was that of many of his successors in this field. He made no attempt to quantify the potentials with rotations of the eyes.

Meyers[15] (1929), like Schott, used an electrocardiograph to study the movements of nystagmus. He claimed that his technic required horseshoe-shaped tin electrodes on gauze saturated in saline solution and held on by tight bandages. He was the first to record eye movements with the lids closed. Meyers regarded his records as originating from the action potentials of the extraocular muscles.

As part of a research program investigating the relation of mental activity and relaxation to neuromuscular potentials, Jacobson[16] (1930) considered ocular movement. Electrodes were of 1 by 2 cm. platinum foil and were wrapped in cotton soaked in isotonic sodium chloride solution. One was placed above the medial portion of the right orbital ridge; the other, over the right mastoid bone. The electrodes were covered to prevent evaporation and held to the skin with gummed paper.

Jacobson found that if the mastoid electrode was changed to the temple he got larger potentials, but he claimed that with the latter placement the currents were

14. Schott, E.: Über die Registrierung des Nystagmus und anderer Augenbewegungen vermittels des Saitengalvanometers, Deutsches Arch. f. Klin. Med. **140**:79-90, 1922.

15. Meyers, I. L.: Electronystagmography: A Graphic Study of the Action Currents in Nystagmus, Arch. Neurol. & Psychiat. **21**:901-918 (April) 1929.

16. Jacobson, E.: Electrical Measurements of Neuromuscular States During Mental Activities: I. Imagination of Movement Involving Skeletal Muscle, Am. J. Physiol. **91**:567-608, 1930; III. Visual Imagination and Recollection, ibid. **95**:694-702, 1930.

not monophasic (fitting his results to the erroneous theory that he was dealing with action potentials of the extraocular muscles).[17] His assertion that there were changes of potential with willed relaxation of the eye would lead one to believe that the standing potential can be varied psychically.

Jacobson was the first in taking the electro-oculogram to use a vacuum tube amplifier. His difficulty was that he used an alternating current amplifier.[18] He did not know he was dealing with a standing potential but thought he was recording action potentials from the extraocular muscles.[19]

The renascence of the standing potential came with the work of Mowrer, Ruch and Miller.[20] They were able to obtain the results of Meyers and of Jacobson, but their explanation was not one of action currents of eye muscles. Using a direct current amplifier and a ballistic galvanometer, they picked up potentials with silver-silver chloride electrodes in isotonic sodium chloride solution. They noticed that eye movements in the plane of the electrodes gave galvanometric changes, whereas movements at right angles to this plane gave none. They also perceived that Meyers' graphs did not have the jagged appearance of electromyograms but, instead, presented smoothly sustained potentials. In a well designed series of experiments, they made the following observations:

1. The greater the rotation of the eye, the greater the potential (for extreme version, 0.5 to 0.75 millivolt).

2. The electrode nearer the retina (not the electrode nearer the contracted muscle), was the more negative one.

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17. If one electrode is placed on or near electrically active tissue and the other (indifferent or distal) electrode on electrically inactive tissue, the recorded action potential is known as a monophasic potential. When both electrodes are on or near the same active tissue, a wave of electricity causes the two electrodes to be first negative and then positive, or vice versa, with respect to each other. The resulting wave form is described as a diphasic potential (Curtis, H. J., and Cole, K. S.: Nerve: Excitation and Propagation, in Medical Physics, edited by Otto Glasser, Chicago, The Year Book Publishers, Inc., 1944, pp. 798-807). Since the standing potential of the eye is not an action potential, this terminology does not apply to the electrical recording of eye movement.

18. The alternating current vacuum tube amplifier can increase signals of short duration (up to one or two seconds, depending on the coupling and its constants) or continuous signals that are chopped up or fluctuating. If the amplification of a continuous and steady potential is desired, a direct current amplifier must be employed. The standing potential, in contrast to the illumination potential, is a constant direct current and therefore requires a direct current amplifier. If an alternating current amplifier is used, as Jacobson has done, a change in the direct current potential in the leads caused by an eye movement may give the appearance of an action current of muscle origin.

19. True action currents of extraocular muscles have been taken, but only by direct application of the electrode on the muscle, never remotely (Hoffmann, P.: Über die Aktionsströme der Augenmuskeln bei Ruhe des Tieres und beim Nystagmus, Arch. f. Anat. u. Physiol., Physiologische Abteilung, 1913, pp. 23-34. Köllner, H., and Hoffmann, P.: Der Einfluss des Vestibulärapparats auf die Innervation der Augenmuskeln, Arch. f. Augenh. **90**: 170-194, 1921; ibid. **92**:272-281, 1923. Perez-Cirera, R.: Untersuchungen über die Aktionsströme der Augenmuskeln mit Hilfe von Verstärkern, ibid. **105**:453-459, 1932). Their use, then, is limited with human subjects.

20. Mowrer, O. H.; Ruch, T. C., and Miller, N. E.: The Corneo-Retinal Potential Difference as the Basis of the Galvanometric Method of Recording Eye Movements, Am. J. Physiol. **114**:423-428, 1936; footnote 6.

3. Passive movement of the eye (the muscles not contracting) in anesthetized cats gave virtually identical results with voluntary movements in human subjects.

4. There were no changes of potential with eye movements after chemical destruction of the retina in cats.

5. Direct evidence of a standing potential was obtained in a freshly excised turtle eye.

After their investigation, but before its publication, Mowrer, Ruch and Miller found a review by Kohlrausch [8] (1931) of the abundant research done on the standing potential during the previous half-century.

If the eye is constantly and truly polarized and the surrounding tissues have a homogeneous conductance, the potential picked up should have a fixed relation to the angle of rotation of the globe. There is a simple, crude analogy to the rotation of a magnet in a coil of wire, where the electromotive force produced is proportional to the sine of the angle of rotation. Fenn and Hursh [21] (1937) were the first to show quantitative agreement with the sine formula. Moreover, they used large angles of rotation—about 70 degrees.

The subject was seated about 3 M. from a wall, which was blank except for fixation points, and fixated a point directly ahead. Then a series of points to the right and the left were successively fixated, back and forth. The deflections of a string galvanometer were averaged from a number of records. Unhappily, neither a measure of the dispersion of the points which make each single point on the graph nor even the exact number of records averaged is given. One, therefore, cannot tell the accuracy and the precision of the electro-oculogram from the report of this investigation. Incidentally, no mention is made of the type of electrode employed.

Chart 1 is redrawn from Fenn and Hursh. Note that when the eye is turned through the angle α a straight line is obtained by plotting millivolts against the sine function of α ($2 \sin \alpha/2$). Fenn and Hursh found, further, that for any one subject the potential is quite constant. Among subjects it varied from 0.2 to 0.8 millivolt. With 21 subjects they were not able to correlate the potentials (or actually the slopes of the curves on the graph, which can be used as a measure of the standing potential) with age, sex or other characteristics. The results of their experiments on eye movement with the lids closed are interesting but beyond the compass of this review.

Halstead [22] tested the electro-oculogram. Using a three stage alternating current amplifier with a direct-writing oscillograph, he confirmed the constancy of the potential in individual subjects. He claimed that movement could be recorded within an angle of $\pm$ 1 degree. Small silver electrodes were used.

Next to appear in the field was a spate of papers by Miles [23] (1938, 1939, 1940). For electrodes he used small metal foil disks with a thin layer of salt paste. The

21. Fenn, W. O., and Hursh, J. B.: Movements of the Eyes When the Lids Are Closed, Am. J. Physiol. **118**:8-14, 1937.

22. Halstead, W. C.: A Method for the Quantitative Recording of Eye Movements, J. Psychol. **6**:177-180, 1938.

23. Miles, W. R.: The Polarity Potential of the Human Eye, abstracted, Science **88**:437, 1938; Einthoven String Galvanometer Used with a Vacuum Tube Microvoltmeter, Rev. Scient. Instruments **10**:134-136, 1939; The Steady Polarity Potential of the Human Eye, Proc.

(Footnote continued on next page)

foil was held on by bits of adhesive tape. Wires led to a direct current amplifier (vacuum tube voltmeter) and then into a string galvanometer.

Miles standardized the measurement of potentials for the purpose of comparison among subjects and under various conditions in individual subjects. He took measurements over an 80 degree range of rotation at 150 cm. and agreed with Fenn and Hursh that the potential is a sine function of the angle of rotation. Arbitrarily he set a lateral angle of 30 degrees, whose sine equals ½, as the

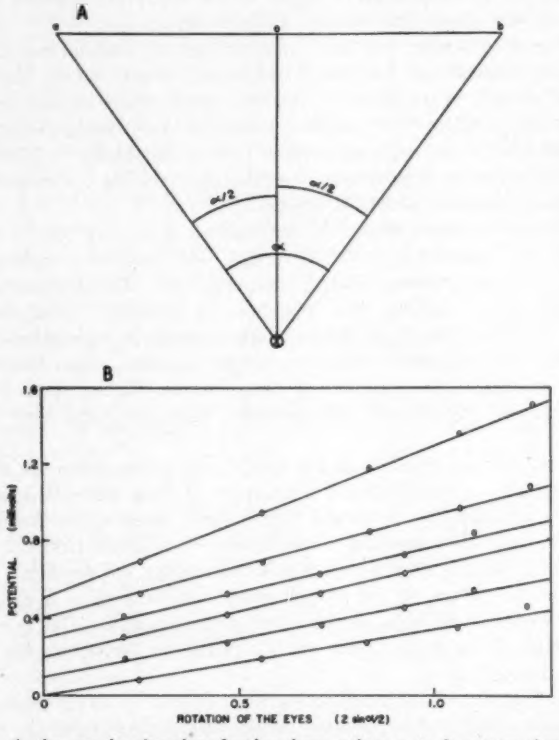

Chart 1.—*A*, the eye in changing fixation from points *a* to *b* rotates through angle α. Sin α = 2 sin α/2. *B*, graphs of six subjects showing that the potential is directly related to the equation sin α = 2 sin α/2. Each curve is plotted 0.1 millivolt above the one below to avoid confusion. All graphs actually begin at zero. (After Fenn and Hursh[21]).

Nat. Acad. Sc. **25**:25-36, 1939; Reliability of Measurements of the Steady Polarity Potential of the Eye, ibid. **25**:128-137, 1939; Performance of the Einthoven Galvanometer with Input Through a Vacuum Tube Microvoltmeter, J. Exper. Psychol. **25**:76-90, 1939; The Steady Potential of the Human Eye in Subjects with Unilateral Enucleation, Proc. Nat. Acad. Sc. **25**:349-358, 1939, abstracted, Science **89**:403, 1939; Influence of Pressure and Other Factors on the Polarity Potential of the Human Eye, abstracted, Psychol. Bull. **36**:536, 1939; Experimental Modification of the Polarity Potential of the Human Eye, Yale J. Biol. & Med. **12**:161-183, 1939, abstracted, Science **90**:404, 1939; Modification of the Human-Eye Potential by Dark and Light Adaptation, abstracted, Science **91**:456, 1940.

standard. Using this pattern, i. e., the potential difference from the central position to a 30 degree fixation to one side, he found much of interest. Subjects show from 0.2 to 2.5 millivolt for each eye. Emotional activity causes rapid change in potentials, which may amount to several millivolts and upsets zeroizing. This is the well known psychogalvanic reflex.[24] The potential to be zeroized (sum of the body potentials) may run from zero to ± 100 millivolts; ordinarily it is constant or changes very slowly and therefore does not seriously interfere. There is no correlation between this body potential after it is balanced and the standard eye potential, but it is not known whether there is any relation before balancing. There is a consistent tendency for eye potentials to be slightly lower on the second day, probably due to a reduction of apprehension and indicating a psychic effect on the standing potential of the eye.

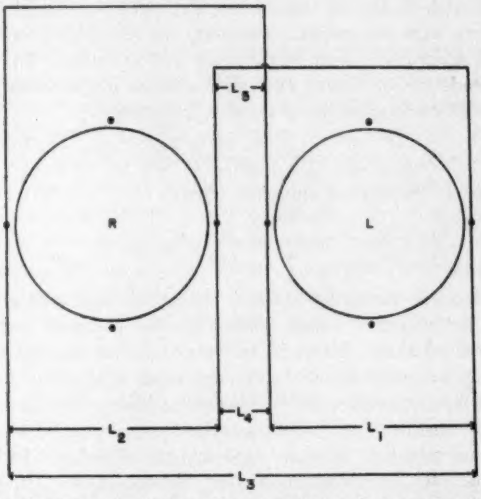

Chart 2.—Schematic diagram of the various leads designated and investigated by Miles.[23] *R* represents the right eye and *L* the left eye. Some leads cannot be used simultaneously with certain others because a short circuit would result, e. g., L_6 with $L_1 + L_4$. No vertical leads are shown.

In the horizontal standardization of leads, Miles used the following designations, illustrated in chart 2: L_1, across the left eye; L_2, across the right eye; L_3, bitemporal leads; L_4, binasal leads; L_5, L_1 and L_2 in parallel. The following relationships were found generally true:

$$L_1 + L_2 = L_3 + L_4 \text{ or } L_1 + L_2 - L_4 = L_3$$
$$L_3 = \tfrac{1}{2}(L_3 + L_4) \text{ and } L_4 = \tfrac{1}{2}(L_1 + L_2)$$

24. The psychogalvanic reflex, or galvanic skin response, is an evanescent decrease of skin resistance after a psychic stimulus, such as surprise or fright. It is believed to be mediated by the sympathetic division of the autonomic nervous system through its control of sudation and vasodilation. Its effect may easily be distinguished from other changes in potential by controlling the stimulus and by its latent period of three to five seconds and its duration of three to 15 seconds (Landis, C.: Electrical Phenomena of the Skin: Galvanic Skin Response, Psychol. Bull. **29**:693-752, 1932).

From these equations it is apparent that there are electric fields about the eyes; if one were, instead, dealing with simple linear conduction, then

$$L_1 + L_2 = L_3 - L_4$$

Next, Miles took nine subjects with unilateral enucleations and compared their steady potentials with those of normal subjects. He noted that in the normal eye the potential is larger when the eye is turned temporalward than nasalward. The difference, usually about 8 per cent, was also found to hold for the group with enucleation. The most likely reason for this discrepancy was the inability to place electrodes symmetrically in the same frontal plane. Other possible reasons were the lack of uniformity of the distribution of potential over the globe and of conduction in the surrounding tissues. Generally, for the same reason(s), a larger voltage is found when the eye is directed upward than downward.

In the group with unilateral enucleation, the electrification about the artificial eye seemed to vary with the individual subject, and the electric field radiated from the active eye in accordance with its direction and distance. The usual formulas for the various leads are, of course, not valid with one eye missing. The following expressions were given to meet the changed circumstances:

$$L_1 \neq L_2 \quad L_3 < L_{\text{active eye}} \text{ (1 or 2)}$$

$$L_{\text{active eye}} - L_{\text{artificial eye}} + L_4 = L_3$$

This is in contrast to the normal situation, where

$$\frac{L_1 + L_2}{2} = \frac{3}{4} \cdot L_3$$

Individual differences in the spread of the electrical field appeared to be pronounced.

Miles found the effect of other factors on the potential recorded with his standard 30 degree rotation. About 15 seconds of digital massage of the closed lid raised the standard potential a statistically significant 0.07 millivolt. A few drops of 10 per cent sodium chloride solution (isotonic sodium chloride is, of course, 0.9 per cent solution) instilled into the conjunctival sac increased the potential 0.37 millivolt for several minutes. It was found that the closed eye had a slightly, but statistically significantly, higher potential than the open one. The potential of the eye increases with apprehension and decreases with relaxation, but this effect was minimized as a factor by the time of the subject's third visit. A change in illumination from darkness or 0.001 millilambert to 5 millilamberts gave a change of 0.38 millivolt in potential, which was statistically valid. The change in voltage occurred over a period of five minutes, with most of the alteration in the last two minutes. All these effects do not necessarily originate from the site of the standing potential of the eye but may occur in the surrounding tissues.

At about the same time as this prolific research of Miles was published, Hoffman, Wellman and Carmichael [25] reported on a quantitative comparison of the electrical and photographic technics of eye movement recording. The electrodes were of flat solder drops about 4 mm. in diameter and attached by circles of adhesive plaster. Skin contact was aided with commercial electrode jelly. An alternating current amplifier was used. Various combinations of vertical and horizontal leads

25. Hoffman, A. C.; Wellman, B., and Carmichael, L.: A Quantitative Comparison of the Electrical and Photographic Techniques of Eye-Movement Recording, J. Exper. Psychol. **24**:40-53, 1939.

were tried. Bitemporal leads were found best because they gave the largest voltage. Maximum rotations were about 12 degrees at a fixation distance of 30 cm. Ten excursions were made in the horizontal and 10 in the vertical plane, and the averages for the horizontal excursions were correlated with photographs, which were taken in the horizontal plane only. For these small excursions they found a linear function for voltage against linear distance of fixation in the target plane. This means that for the 12 degree excursion the potential was a linear function of the tangent of the angle of rotation.

At the same time, in France, Baudouin, Fischgold, Caussé and Lerique [26] (1939) briefly reviewed the subject. They made tracings of optokinetic nystagmus, employing electroencephalographic equipment. They used silver-silver chloride electrodes in isotonic sodium chloride solution, which was held in position by a small bell-shaped rubber container whose mouth was cemented to the skin (Baudouin, Fischgold and Lerique [27]).

During the same year, the electrical potential in eye movement was being investigated in Germany. Jung [28] was interested in nystagmus. He recorded the vertical and horizontal movements of each eye, using an electrocardiograph with an alternating current amplifier. The electrodes were mushroom shaped and of not more than 10 mm. diameter. Moistened with isotonic sodium chloride solution, they were placed exactly in a horizontal or vertical plane intersecting the center of the eye. Indifferent electrodes were attached to the ears. The electrodes about the eyes were held in place by goggles, whose lenses, incidentally, prevented fixation for the nystagmus experiments. The leads were used from each eye separately, but bitemporal leads were used too. Jung well realized the limitations of the alternating current amplifier and took pains to point out how it differed from its direct current counterpart.

Jung maintained that the electrical method was limited in accuracy to 5 degrees, in contrast to the ± 1 degree of Halstead.[22] Furthermore, he continued, higher amplification would bring out action potentials of the eye musculature. With one electrode on the ear, common brain waves of about 10 cycles per second (Berger, or alpha rhythm) were picked up. Another possible source of error, he went on, was the psychogalvanic reflex. Jung applied his recording to analyses of physiological and pathological nystagmus (Jung [29]; Jung and Mittermaier [30]).

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26. Baudouin, A.; Fischgold, H.; Caussé, R., and Lerique, J.: Une vieille notion trop oubliée: I. La différence de potentiel rétino-cornéenne; son intérêt théorique et pratique, Bull. Acad. de méd. **121**:688-693, 1939.

27. Baudouin, A.; Fischgold, H., and Lerique, J.: Une nouvelle électrode liquide, Compt. rend. Soc. de biol. **127**:1221-1222, 1938.

28. Jung, R.: Eine elektrische Methode zur mehrfachen Registrierung von Augenbewegungen und Nystagmus, Klin. Wchnschr. **18**:21-24, 1939.

29. Jung, R.: Ein Apparat zur mehrfachen Registrierung von Tätigkeit und Funktionen des animalen und vegetativen Nervensystems (Elektrencephalogramm, Elektrokardiogramm, Muskelaktionsströme, Augenbewegungen, galvanischer Hautreflex, Plethysmogramm, Liquordruck und Atmung), Ztschr. f. d. ges. Neurol. u. Psychiat. **165**:374-397, 1939.

30. Jung, R., and Mittermaier, R.: Zur objektiven Registrierung und Analyse verschiedener Nystagmusformen: Vestibulärer, optokinetischer und spontaner Nystagmus in ihren Wechselbeziehungen, Ztschr. f. Hals-, Nasen- u. Ohrenh. **46**:320-323, 1939; abstracted, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **146**:410-439, 1939.

Lindsley and Hunter [31] (1939) recorded eye movements from four pairs of electrodes simultaneously. These were hatlike, chloridized silver electrodes with an inside diameter of 5 mm. and were attached with collodion. Electrode jelly was injected through a hole in the dome of the hat. The signals were fed into an alternating current amplifier and optical oscillograph. Apparently, these authors, like Jung, were annoyed with muscle action potentials.

> The records reveal muscle action potentials; but the great swings in potentials do not arise from such a source. . . . Furthermore, unpublished observations by one of us, Lindsley, using direct recording of action potentials of the exposed human extraocular muscles indicates that such muscle potentials are of the typical rapidly fluctuating type. The magnitude of such potentials, even from the exposed muscles, is not so great as those recorded here from the margins of the orbit.[31]

Here, then, is evidence that the action currents of the extraocular muscles cannot ordinarily be picked up remotely.

Because of their interest in nystagmus, Perlman and Case [32] (1939) recorded eye movements electrically. For electrodes they used silver disks with electrode paste; for recording they used an alternating current amplifier with an ink-writing oscillograph. Their findings were about what would be expected from the previous literature.

> . . . Note that the displacement of the writing arm for an eye movement of 24 degrees is twice that for an eye movement of 12 degrees. An angular deviation as small as two degrees can be detected.[32]

In contrast to the claimed 5 degree maximum precision of Jung, Perlman and Case [32] said that calibration with 6 degree movement is very clear. However, they believed that they also got action currents from the extrinsic muscles, as evidenced by a sharp spike of the quick component. They mentioned nothing about possibly significant inertia of the ink writer.

There is yet one more paper on which to report to complete the bountiful harvest of 1939. The investigation was done in Sweden by Leksell.[33] He used a direct current amplifier with an optically recording oscillograph. His electrodes were patterned after those of Baudouin, Fischgold and Lerique [27] except that they were held on by suction, in lieu of rubber cement. The indifferent electrode was placed on the forearm.

> If the oscillograph deflections corresponding to horizontal eye-movements are plotted in mm. against the sine of the subtended angle α an approximately straight line is obtained, in agreement with Fenn and Hursh. However, if the sine of α is replaced with α itself equally straight lines are obtained. This means that from a practical point of view the oscillograph deflections for horizontal eye-movements up to 45° from the median position may be considered as directly proportional to the angle of deviation of the eyes.

A graph redrawn from Leksell is given in chart 3. This is one of three equally good examples which he offers comparing the linearity of the two functions. The

31. Lindsley, D. B., and Hunter, W. S.: A Note on the Polarity Potentials from the Human Eye, Proc. Nat. Acad. Sc. **25**:180-183, 1939.

32. Perlman, H. B., and Case, T. J.: Nystagmus: Some Observations Based on an Electrical Method for Recording Eye Movements, Laryngoscope **49**:217-228, 1939.

33. Leksell, L.: Clinical Recording of Eye-Movements, Acta chir. Scandinav. **82**:262-270, 1939.

potential is presumed to be directly proportional to the deflection of the galvanometer in millimeters, as shown on the ordinates.

Lyman [34] (1941) noted traces of eye movement with his electroencephalograph, which is essentially a high gain alternating current amplifier. He noted that with the low amplification used for registration of eye movements the brain waves did not appear except in a high voltage discharge, such as occurs in some epileptic attacks.

Luckiesh and Moss [35] (1941, 1942) discussed the use of electro-oculograms in the study of reading. They erroneously called the tracings electromyograms. Apparently, they had not read any of the literature on electro-oculography for the previous six years, which was unanimous only in the statement that muscle action potentials were not involved.

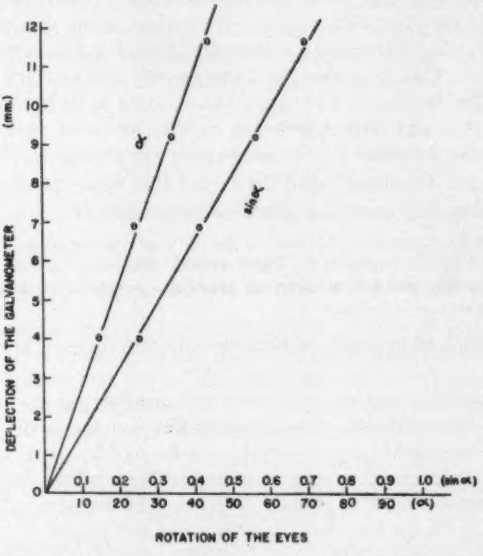

Chart 3.—Good linearity is found regardless of whether sin α or the actual angle α is used. Leksell demonstrates this fact with the curves for three subjects, which are equally convincing. One of the graphs has been redrawn here. (After Leksell.[33])

The urgency of the war years left a gap in the chronology of this literature. Soon afterward, Redlich, Callahan and Schmetje [36] (1946) published their investigation on 40 patients with injuries and diseases of the eye and its adnexa. Their

34. Lyman, R. S.: Eye Movements in the Electroencephalogram, Bull. Johns Hopkins Hosp. **68**:1-31, 1941.

35. Luckiesh, M., and Moss, F. K.: Reading a Line of Print, School & Soc. **53**:612-615, 1941; Reading as a Visual Task, New York, D. Van Nostrand Company, Inc., 1942, pp. 16 and 387.

36. Redlich, F. C.; Callahan, A., and Schmetje, J. F.: Electrical Potentials from Eye Movements, Yale J. Biol. & Med. **18**:269-274, 1946.

findings were completely consistent with those of Mowrer, Ruch and Miller, since they, too, found no potential without a retina, although it was present in retinas blinded by disease.

> Typical potentials after blinking and other eye movements could be obtained from normal eyes and from blind eyes due to optic nerve disease and retinopathies. They could not be obtained on the affected side in patients with enucleations and eviscerations.[36]

In addition, they reported that electrical recording is not suitable for slight eye movement but did not offer any quantitative limitation. The same work is referred to by Callahan and Redlich [37] (1946).

In their research on reading and visual fatigue, Carmichael and Dearborn [38] (1947) recorded eye movement, among other functions, electrically. They used largely the procedures and equipment of Hoffman, Wellman and Carmichael.[25] Some refinements were added. Before the hat-shaped, chloridized silver electrodes were fastened to the skin with collodion, the surface of the skin was cleansed with ether. The skin was irritated with a toothpick through a hole in the dome to insure adequate contact. Then a commercial electrode jelly (an agar and acid compound) was applied. The resistance of the skin was required to be not over 10,000 ohms. If it was, the skin was further irritated, or the electrodes were reapplied. The alternating current amplifier was coupled to an ink-writing oscillograph.

Carmichael and Dearborn called the record they made an electro-oculogram.[39] For their purpose, they made the definition rather narrow.

> The term electro-oculogram in this book is used to apply to the records traced in ink upon the recording used in the experiment. These records are made, as indicated above, by an ink-writing oscillograph which is actuated by amplified currents originating in the electrodes placed about the orbits of the eyes.[38]

Their records obtained in reading a book or microfilm covered, of course, relatively small angles.[40]

The latest, perhaps the most fascinating and probably the most ingenious application of electro-oculography has been made by Powsner and Lion [41] (1950). Their electronic recordings show the concerted force exerted by the extraocular muscles acting together to produce an eye movement. Their electrodes consist of cup-shaped silver buttons about 3/16 inch (4.8 mm.) in diameter. They are held in place bitemporally by the head band from a set of ear phones.

The potential is amplified through a direct current amplifier to an oscillograph, which gives what might be called the direct function. This is the angular position

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37. Callahan, A., and Redlich, F. C.: Electroencephalography and Ophthalmology, Am. J. Ophth. **29**:1522-1533, 1946.

38. Carmichael, L., and Dearborn, W. F.: Reading and Visual Fatigue, Boston, Houghton Mifflin Company, 1947.

39. In this review, "electro-oculogram" is used to refer to the record of eye movements found by a change of potentials about the orbit of the eye and is not limited to a specific type of instrument. In accordance with Hans Berger's terminology for brain waves, *-gram* is the recording, *-graph* the recording apparatus and *-graphy* the technic.

40. A motion picture film showing the equipment and procedure in color or black and white is available for rent or sale (Mead, L. C., and Carmichael, L.: The Electrical Recording of Eye Movements, Psychological Cinema Register of Pennsylvania State College, no. PCR-75K [not dated]).

41. Powsner, E. R., and Lion, K. S.: Testing Eye Muscles, Electronics **23**:96-99, 1950.

of the eyeball as a function of time, $\theta\ (t)$. If this voltage were to be mathematically differentiated by the use of the calculus, the resulting graph would show the velocity of eye movement.

$$\omega = \theta\ (t)/dt.$$

This is done, but it is done electronically, so that another oscillograph gives the velocity function. The velocity function is differentiated, giving the angular acceleration of the eyeball (second derivative of the original direct function),

$$a = d^2\ \theta\ (t)/dt^2$$

and this is recorded on a third oscillograph.

For translational (linear) movement, force is equal to mass times acceleration, according to Newton's second law of motion. This may be written as $T = a\ I$ for rotational (angular) movement, where T is the torque, a the angular acceleration and I the polar moment of inertia of the eyeball. It can also be shown that $T = fr$, where f is force and r is the radius at which the force is applied.

Allowing that the torque, T, is the result of the extrocular muscle force, f, acting at radius r from the center of rotation, the muscular force can be found from the equation:

$$f = \frac{T}{r} = \frac{aI}{r} = \frac{d^2\ \theta\ (t)}{dt^2} \cdot \frac{I}{r}$$

The output voltage is proportional to the angular position of the eye, so that

$$f = k \frac{d^2\ \theta}{dt^2} \cdot \frac{I}{r}, \text{ or } f = C \frac{d^2\ \theta}{dt^2}$$

Therefore the muscular force, f, of the extraocular muscles is proportional to the second derivative of the output voltage (acceleration of eye rotation). The values k, I and r are constants and can be reasonably approximated or determined when necessary for absolute measurements. When relative measurements are desired, these constants may be lumped in another single constant, C.

Lion and Powsner [42] reported a linear relationship between rotation of the eyes and the potential measured, which contrasts with the results of Fenn and Hursh.[21] They also report an interesting phenomenon.

> Preceding each movement there is a small spike in the opposite direction of about 10 microvolts. This would correspond to a retrograde motion of the eye through 2 degrees, or it may represent a muscle twitch connected with eye movement.[42]

Further, they found that the starting and stopping of eye movements in the central field is abrupt, whereas in the periphery it is more gradual. The force of the extraocular muscles in turning the eye varies from 280 dynes, for a saccadic reading movement, to 470 dynes, for the return sweep.

Continuing this investigation, Brockhurst and Lion [43] found that the velocity of eye movement follows the all or none principle when a subject moves his eyes through an angle of 90 degrees; that is, the maximum velocity remains

42. Lion, K. S., and Powsner, E.: A New Ergographic Method for Testing the Ocular Muscles, to be published.

43. Brockhurst, R. J., and Lion, K. S.: Study of Normal Ocular Movements, to be published.

essentially constant. It was not found possible to reduce the maximum velocity of the eye voluntarily; they could only split the movement into several separate saccades, each having the same maximum velocity as that of the original single sweep.

Lion and Brockhurst [44] next devised a "stress test," whereby two fixation lights, 90 degrees apart, flashed alternately at a rate of 120 to 150 changes per minute. No decrement of acceleration was found; that is, there was no fatigue of the neuromuscular apparatus, Failure in performance consisted of a decreased excursion or an inability to respond to the rhythm of the stimulus.

THE ELECTRO-OCULOGRAM AND ITS USES

It has been seen how the electro-oculogram can be and is used in the recording of eye movement in nystagmus, in reading and with the eyes closed. What other possibilities does this technic have in research and in clinical investigation?

First, some of its limitations have been indicated. No information is gained directly from the extrinsic muscles of the eye, since their action potentials are not picked up with remote leads. The best estimate, though it is not a statistical one, and is therefore rather crude, confines the precision to $\pm$ 1 degree. Although such temporal factors as apprehension and skin resistance may change the potential input to the amplifier, a rapid and very simple recalibration will prevent any error from such sources. Amplifiers and oscilloscopes worthy of use in careful investigation are expensive.

Many optimistic predictions or suggestions have been made for the future of electro-oculography in visual research. Most of them have not yet been fulfilled or followed. Halstead [22] has given his enthusiastic list.

> While presumably the method is applicable in any investigation where the problem of detecting eye movements is involved, the following are examples of some of the various types of investigations for which we find the method to be well suited: The direct control of fixation in mapping central and peripheral visual fields, eye movements in cases with aphasia, eye movements associated with Phi and autokinetic phenomena, the study of pseudo-hallucinations, fantasy and imagination, nystagmic reactions of various types, reading and others. In addition, it should prove feasible to use the method in connection with discrimination experiments involving subhuman animals.[22]

Hoffman, Wellman and Carmichael [25] had a more limited list.

> It [electro-oculography] makes possible the study of the reflex adjustments and reactions of the eye in a totally dark room or in an experimental situation such as that required for the study of the autokinetic phenomenon in which a stimulus light of low intensity must be used. Movements of the eyes in emotional situations and in experiments whose procedure requires the subject to move his head or indeed his whole body may now be more normally and conveniently studied. This is possible because of the relative absence of restraint and interfering apparatus required by the electrical technique. It has, for example, suggested itself to the authors that eye-movements of a motorist while driving in various traffic situations could be measured by this technique, although a number of special electrical details would have to be worked out before such registration would be possible. The electrical technique of eye-movement recording can also be used with young infants and with animals. One of the present writers has indeed participated in preliminary experiments using this method of recording the eye-movement of young infants in a rotating drum such as to bring about optokinetic nystagmus.

44. Lion, K. S., and Brockhurst, R. J.: Study of Ocular Movements under Stress, to be published.

The conditions of this experiment suggest that the technique may be adapted so as to form an objective method of studying quantitatively the degree of "night blindness" resulting from Vitamin A deficiency even in newborn human infants.

Carmichael and Dearborn [38] (1947) reported that one of them (L. C.) had been interested in the use of electro-oculograms in the study of fetal and newborn guinea pigs and rabbits.

There remains much that could be investigated using the electro-oculograph as an instrument of research, and even possibly of clinical study. The dispersion of the voltage from its straight line plot (found by the method of least squares) should be measured. This would be the standard deviation for many rotations of various degrees in a number of subjects. The points would not be averaged before the dispersion was found. Then the average standard deviation for various subjects and its deviation could be found. Given these data, one would be in a position to know the precision of electro-oculograms in terms of probability, rather than the present ranges (from $\pm$ 1 degree to not better than 5 degrees). Since Lion and Powsner [44] have reported that 10 microvolts corresponds to about 2 degrees of rotation, the ultimate precision should be considerably better than 2 degrees. This should be determined for both bitemporal and monocular leads over large conjugate movements of the eyes.

Next, the same should be done for disjunctive ocular movements, especially for convergence and divergence. Actually, there is no report in the literature of disjunctive movements studied with the electro-oculogram, although some of the authors cited earlier (notably, Jung [28]) have not only mentioned the possibility but also had the equipment and leads arranged to record them. Disjunctive registration requires a separate pair of leads and a separate amplifier channel for each eye for the horizontal meridian and a duplicate set of apparatus for the vertical meridian if a simultaneous record is desired. Incidentally, it is noted that symmetrical disjunctive movements should not register at all with bitemporal leads if both eyes are equal electrically.

Once the capabilities and limitations of disjunctive movements are known, a whole new field of possibilities is open in the use of electro-oculography in clinical research. This topic will be covered elsewhere.

SUMMARY

Corneoretinal potentials and the subclassifications of standing potential and illumination potential are discussed. Attention is called to the incorrect trend in the American literature in which the term "corneoretinal potential" is used in lieu of "standing potential." The origin of the standing potential and its relation to the illumination potential are reviewed.

The history and development of the use of the standing potential in the registration of eye movement are critically reviewed in detail. Finally, some possible uses of the technic are covered and suggestions for further research made.

THE TROPOPHOROMETER

An Instrument Employing a New System of Coordinates for More Accurate Measurements of Heterophoria and Heterotropia

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AND
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A TROPOPHOROMETER (fig. 1) was devised in 1944 [1] for the purpose of permitting measurements of extraocular muscle anomalies in the six cardinal directions by any of the methods in which a heterotropia or heterophoria is usually measured. The instrument consisted of two lights mounted in such a way that each moved as though it were traveling over the surface of a sphere which had for its center the center of rotation of the eye. In addition, each light was shielded so that it could be seen only by the eye around whose center of rotation the light moved. The distance of the lights from the eye was about 15 inches (38 cm.).

With this instrument the lights were used for fixation while the cover test was being performed; while each eye fixed its corresponding light, the lights were moved manually until, when the cover was passed back and forth from one eye to the other, there was no longer any movement of the eyes. This test could be made in any position the eyes were capable of assuming. It was as easy to measure the deviation laterally as straight ahead; accurate measurements of hyperphoria of as little as 0.25 degree could be made far into the oblique directions. After the movement of the eyes had been neutralized, by adjusting the positions of the lights during the cover test, it was necessary only to read the amount of vertical heterotropia or heterophoria from the vertical scales and the lateral heterotropia or heterophoria from a differential lateral scale. In addition to its use with the cover test, the instrument could be used with the Maddox rod; the red glass with complementary colors, such as red and green, with a filter over the eyes; the screen and parallax test, with cover or by alternate flashing; the Hirschberg test, and tests similar to the von Graefe prism diplopia test. It could be used to detect abnormal retinal correspondence and for mapping out a suppression scotoma.

Comparative measurements could be made at equal distances into the fields of action of the vertically and horizontally acting extraocular muscles, and the identity of the overacting and underacting muscles could thus be established. Measurements could be made for fixation distances from 15 inches to infinity.

For the purposes of comparison and diagnosis, it is important to be able to make measurements some fixed distance into the field of action of the muscles under

1. Putnam, Otto A., and Quereau, J. V. D.: Quereau-Putnam Tropophorometer, Arch. Ophth. **33**:28-31 (Jan.) 1945.

investigation, duplicable not only in each of the cardinal directions but also at subsequent examinations.

This instrument was used for nearly four years, in the measurements of more than 600 patients. It made the rapid determination of the affected muscle, or muscles, in the most complicated types of squint an easy matter. The measurements were always repeatable, with excellent duplication. The hypertropia, found in any cardinal direction, rarely differed by more than 1 degree from the

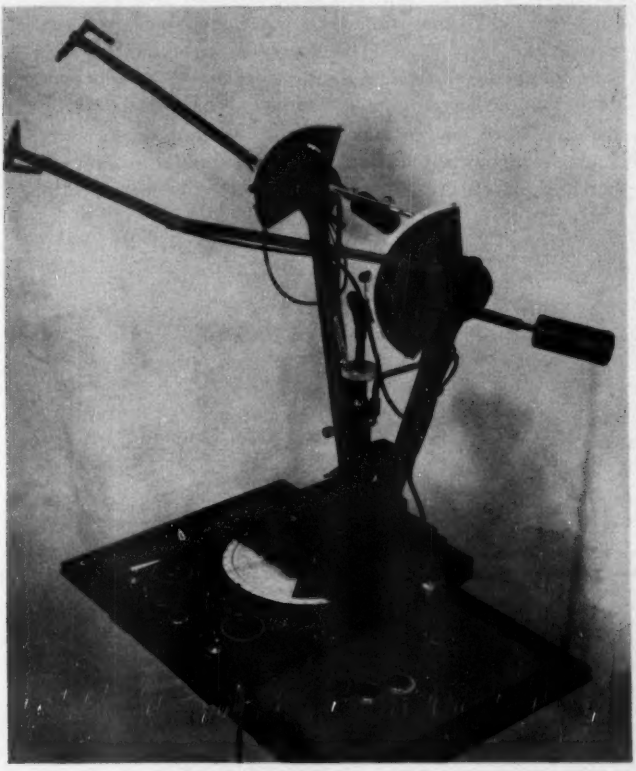

Fig. 1.—First tropophorometer (1944), employing coordinate system *C* (fig. 3).

previous measurements, however large these may have been. These measurements were so constant that patients with myasthenia gravis were easily recognized by the variability of their heterotropias on this instrument.

During the four years this instrument was tested it was found to be the best we had seen for the measurement of ocular deviation. On the other hand, it was found to have certain faults—four in number.

1. Dr. George P. Guibor observed that the fixation lights were too small and recommended larger ones. This observation was found to be correct. Patients

had difficulty in fixing the light, which was only 1.5 mm. in diameter. A lighted target, with lines which required sharper focusing, was found to be more satisfactory.

2. Binocular fixation demands convergence at near fixation distances. This is a normal geometric convergence. Deviation from this normal convergence constitutes a squint. The normal convergence must be added to a divergent squint and subtracted from a convergent squint when an uncompensated scale is used in making the measurement. The amount of this geometric convergence is dependent not only on fixation distance and the interpupillary distance but the direction of gaze as well (fig. 2). The correction for geometric convergence factors was time consuming and led to the development of an automatic computer, which was built into the lateral scale mechanism of a new instrument.

3. In the first instrument it was necessary to read the two vertical scales separately and to subtract their readings in order to find the amount of hypertropia or hyperphoria. Furthermore, a small vertical correction was necessary for near

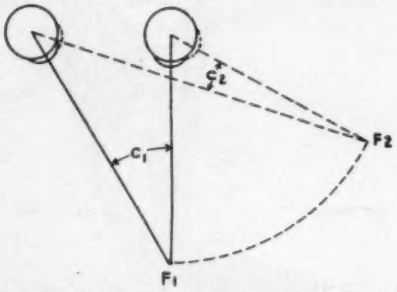

Fig. 2.—The angle of normal geometric convergence changes (C_1 to C_2) as the fixation point moves to either side (left eye fixing). When measured by an instrument with scales, a convergent squint will seem to increase and a divergent squint to decrease with eyes left or right.

readings in the oblique directions because of the fact that the fixation distance was, actually, different for the two eyes. This is apparent in figure 4. A direct reading scale, obviously, was desirable.

4. In 1945 it was discovered [2] that a lateral deviation had a vertical component in oblique directions of gaze. A false hyperphoria was to be found, therefore, in vertical measurements in the oblique cardinal directions when a lateral squint or heterophoria was present.

A critical examination of these faults led to the belief that an instrument, to be of optimum value, must indicate directly, without any computation or allowance whatever, accurate and true readings of both vertical and lateral deviations. With this goal in mind, the above faults were considered. The first two were largely mechanical, and their solution depended on mechanical ingenuity; however, the last two faults led to the theoretical considerations of various possible coordinate

2. Putnam, Otto A., and Quereau, J. V. D.: Precisional Errors in Measurement of Squint and Phoria, Arch. Ophth. **34**:7-15 (July) 1945.

systems. Perhaps a different system of coordinates for expressing direction of the visual lines would be more suitable. If such a system existed, was it accurate and valid?

Figure 3 shows four different representations of possible spherical coordinate systems. These systems are used in locating the direction of a line passing through a fixed point, which in the case in question is the eye. When this line represents the direction of gaze, it is easy to determine its angular relation to the visual line in the eyes front position. It is convenient to express this direction of gaze in terms of a point on the surface of the sphere and the sphere center. *A, B* and *C* of figure 3 are views of the same sphere. These are the lines that would be seen in viewing a globe of the earth held in different positions. *D* is a theoretical possibility but is impractical for reasons deemed irrelevant to this paper.

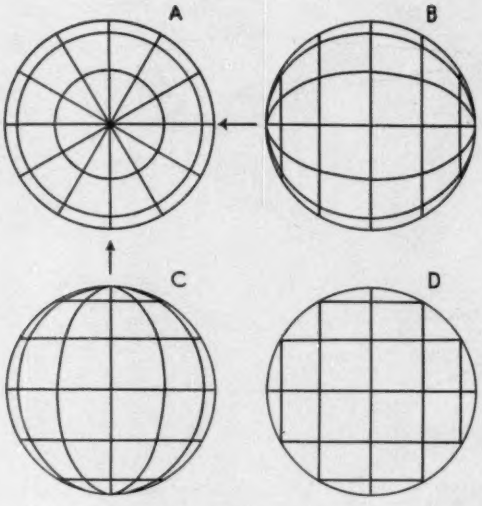

Fig. 3.—Four systems of coordinates.

The perimeter uses system *A*, or the polar coordinate system, and properly so, for here one is measuring the angle formed by a line from the eye to the movable test object and a line constituting the fixed straight-ahead axis. A number of these angular readings are compared in *one* eye to form the visual field. In the case of a squint, it is the difference in the position of the visual lines of the *two* eyes that is measured, requiring a different set of coordinates.

The 1944 tropophorometer used system *C*, as do current versions of the haploscopes and major amblyoscopes. When measuring lateral deviations with coordinate system *C* for binocular fixation of a near target in the oblique cardinal directions, the two eyes do not have identical vertical readings (fig. 4). This difference in vertical readings falsely indicates a hyperphoria, necessitating a correction factor. It is most complicated to correct for the false hyperphoria previously mentioned.

In system *C* (fig. 3) the amount of geometric convergence for near fixations varies with elevation, as well as with lateral direction of gaze.

An investigation of the potentialities of the coordinate system represented by *B* in figure 3 is enlightening. To visualize the application of system *B*, the reader should imagine two such spheres, side by side, each with an eye as center, the axes of the spheres joining end to end to form a common axis passing through both eye centers. In this system, vertical movements of the eyes are expressed, not as the angle of elevation of the visual lines, but as an elevation of the plane of fixation containing these lines, as illustrated in figure 4. In this fact lies the solution to all of the aforementioned difficulties with regard to vertical measurements. Binocular fixation, at any distance and in any direction, has a common vertical reading.

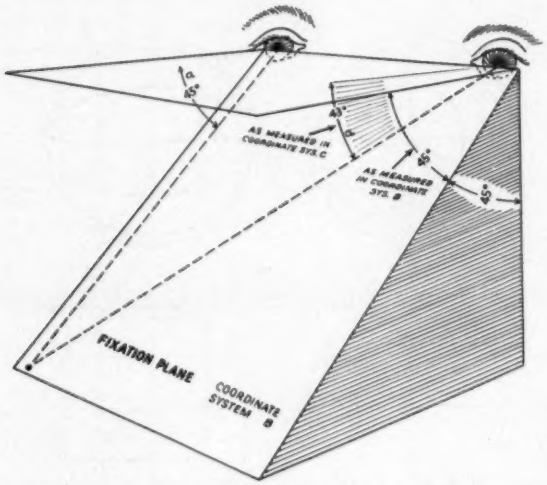

Fig. 4.—In coordinate system *C* of figure 3 (the system in general use) the measurement is made in the vertical plane containing the arrow (*a*) and the visual line. As the left eye turns toward the right in a movement of convergence, the angle of depression, when measured by the arrow (*a*), will become less than the similar angle for the right eye, although both visual lines are in the same plane. If the left eye could rotate 90 degrees to the right, the angle of depression would measure zero. The result is false hyperphoria.

In coordinate system *B* the elevation or depression of the fixation plane (containing the visual lines) is measured, thereby eliminating the false measurement of a vertical component in a lateral deviation.

Any unlike readings represent true hyperphoria or hypertropia. No correction is required, and since the movement in lateral phorias is in the fixation plane rather than in a horizontal plane, there is no problem of false hyperphoria. Finally, in system *B*, the geometric convergence factor is not a function of elevation, as it is in system *C*. Every consideration of theory, accuracy and ease of use favors use of system *B* in future instruments for measuring strabismus. All the geometric faults of the 1944 tropophorometer resulted from what is now known to have been an improper choice of a system of coordinates.

A new tropophorometer (fig. 5) has, therefore, been built with different mechanical axes, so designed that its readings are expressed in coordinate system *B* (fig. 3). Since no correction factor is ever required in vertical readings, the two indicating scales are placed side by side with a differential scale reading directly in both degrees and diopters of vertical deviation. Consequently, faults 3 and 4, listed above, are entirely corrected.

The targets have been redesigned as back-lighted letters slightly larger than the former ones. These letters require more accurate accommodation than the light previously employed. The target holder can be rotated, permitting change to a different type of target, such as from red to black or from fine-lined to coarse-lined

Fig. 5.—New tropophorometer, which employs coordinate system *B* (fig. 3).

targets. By shifting the back light, the target can further be turned to permit straight-through sighting of distant objects for accurate distance measurements.

Nearly two years of effort has resulted finally in an automatic computer for lateral measurements. A single setting feeds the information of target distance and interpupillary distance of the patient into the mechanism, which, furthermore, is linked to both target arms. The amount of geometric convergence is computed automatically for any direction of gaze that is being used; this mechanically determined convergence, in turn, operates a differential scale, permitting direct readings of lateral deviations, which are completely compensated for all geometric convergence factors (fig. 6).

The operation of this instrument, which can measure fixations from infinity to 13 inches (23 cm.), is identical with the operation of the earlier instrument. The

instrument has been in use 18 months prior to this writing. The direct reading feature not only nullifies any chance of mathematical error on the part of the operator but also speeds up the examination.

Vertical measurements are accurate within less than 0.12 degree (½△) in any part of the field of fixation. Lateral measurements have the same accuracy.

Mechanical interference of the two targets is avoided because the fixation distance of each target can be changed as the lights are moved about in the field of binocular fixation. The brightness of the target lights is adjusted by rheostats on the base of the instrument. Single or alternate flashing of target lights is provided for.

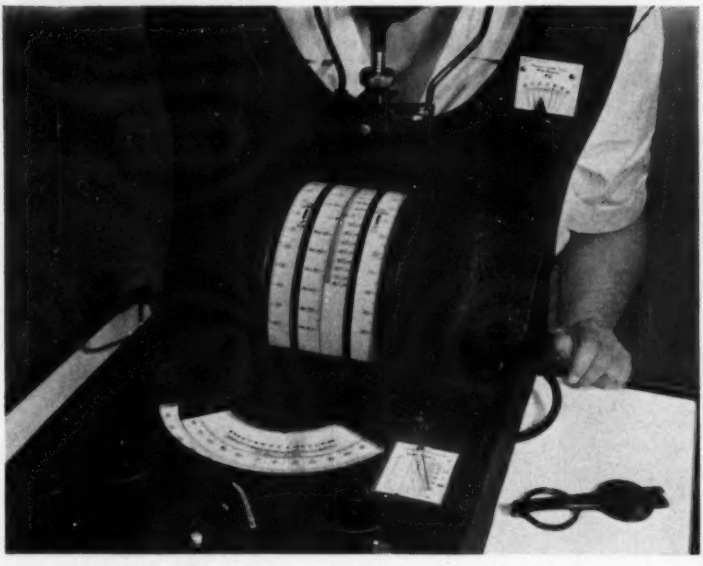

Fig. 6.—Scales and controls for tropophorometer employing coordinate system *B* (fig. 3): Knob (lower left), rheostat for back-lighting scales; button and center pointer switch, for flashing one or alternate target lights; rheostats with numbered dials, left and right foreground, for regulation of target light intensity; differential scale, center of base, for lateral measurements; rectangular scale computer, for automatic scale compensator; differential vertical scales, for measurement of vertical deviations; vernier knobs, on either side of vertical scales, for slight movements of targets by patient in subjective tests.

COMMENT

The tropophorometer permits accurate comparative measurements in all the fields of fixation. It is the ability to compare the measurements made in one direction of fixation with those made in another direction which is essential to the diagnosis of neuromuscular anomalies. In order that a paretic vertically acting muscle be identified, it must be determined in which of the four oblique cardinal directions the hyperphoria or hypertropia is greatest. For laterally acting muscles, comparison of the measurements with eyes right, eyes straight ahead and eyes left

makes possible the diagnosis of the paretic muscle. In cases of convergence excess, divergence insufficiency, convergence insufficiency and divergence excess, the diagnosis is made by comparing the measurement for near with that for distance.

If one measurement, in itself, were the important thing, great accuracy would not be necessary; but since the difference between measurements is of paramount importance, the more accurate the measurement, the more accurate will be the diagnosis, a fact pointed out by Galezowski [3] as early as 1869.

SUMMARY

An instrument built in 1944 for measurement of heterophoria and heterotropia was found to have certain faults due to use of the system of coordinates, which is currently employed in haploscopes and major amblyoscopes.

A new instrument was developed, using a different system of coordinates, which avoids these errors.

It is recommended that this new system of coordinates be employed in future instruments and devices for more accurate measurements of heterophoria and heterotropia.

121 South Seventh Avenue, West Reading (Mr. Putnam).

138 North Fifth Street, Reading (Dr. Quereau).

3. Galezowski, X.: Strabismométrie binoculaire, Ann. d'ocul. **61**:169, 1869.

Clinical Notes

POWER OF THE LACRIMAL LAYER IN THE CORNEAL CONTACT LENS

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NEW YORK

The corneal contact lens is a new type of lens consisting of a small shell, 11 to 12 mm. in diameter, which is applied directly to the cornea. The lens was developed, in part, by the department of ophthalmology of the College of Medical Evangelists, Los Angeles.

The lens is applied to the eye without any solution, and there is only a capillary layer of tears between the lens and the cornea. The inner surface of the lens is made on a slightly longer radius than the radius of the outer surface of the cornea, so that the tears which fill the space between lens and cornea form a concave meniscus lens. The power of this "lacrimal" lens is given by the makers of the contact lens as about — 1.50 D. This does not seem correct, as can be seen by a simple calculation. (The discussion here presented has nothing to do with the merits of the lens pro or con.)

The radius of the outer surface of the cornea is taken as 7.80 mm., and that of the posterior surface of the contact lens, as 8.10 mm. The index of refraction of the cornea is taken as 1.376; the index of the tears, as 1.336, and the index of the plastic used for the contact lens, as 1.488. The power of the "lacrimal" lens can be calculated by taking the sum of its surface powers, since the thickness at the center is negligible.

Each surface power is easily found by my formula $D\text{-}aM$, where D is the dioptric power, a is the difference between the two indexes of refraction (i. e., a equals the amount the second index is above the first index, or $n_2 - n_1$) and M equals the curvature in metric units (i. e., $M = \frac{1{,}000}{r}$, where r is the radius in millimeters).

To find the power of the first, outer surface of the "lacrimal" lens, the index of refraction of the contact lens (n_1) is taken as 1.488; the index of the lacrimal fluid (n_2), as 1.336, and the radius (r), 8.10 mm. Applying these data to the $D\text{-}aM$ formula, we get

$$D = (1.336 - 1.488) \times \frac{1{,}000}{8.10}$$

$$D = -0.152 \times \frac{1{,}000}{8.10} = \frac{-152}{8.10} = -18.77 \text{ D.}$$

For the posterior surface of the "lacrimal" lens, the index of the tears (n_1) is taken as 1.336; the index of the cornea, as 1.376, and the radius of the surface, as 7.80. Applying these data to the $D\text{-}aM$ formula, we get

$$D = (1.376 - 1.336) \times \frac{1{,}000}{7.80}$$

$$D = \frac{40}{7.80} = 5.13 \text{ D}$$

The sum of the two surface powers is — 18.77 D. + 5.13 D. = — 13.64 D.

If the minute thickness at the center, say 0.1 mm., is considered in the calculation, the total power is a little less minus—about — 13.00 D.

The power thus calculated is almost nine times the power as given by the makers of the lens. The power found here is the reduced principal power, as advocated and used by Gullstrand and his followers.

37 West Ninety-Seventh Street (25).

CONVERSION ADAPTER

LORAND V. JOHNSON, M.D.
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I wish to present a conversion adapter which works well in converting the focal length of the light beam of the Poser slit lamp from 75 mm., which is brilliant for the cornea, to 100 mm., such as that provided by the older slit lamps, which allows much better study of the lens and the anterior vitreous. This small converter, which may be simply attached in front of the light beam of the Poser slit lamp, allows one to see the zones in the lens with quite as great clarity as that shown with the older textbooks—but not by the new Poser slit lamp, because of the shorter focal beam.

This instrument is available from the Parsons Optical Service in San Francisco. It is not useful for examination of the cornea; it increases the focal length of the light and is desirable chiefly for examination of the lens or the vitreous.

Read before the Section on Ophthalmology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 29, 1950.

Annual Reviews

CORNEA AND SCLERA

Review of the Literature

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BECAUSE of the great amount and diversity of material on the cornea and sclera published during 1949 and in the early part of 1950, I have selected certain topics and reports that seem to me to have special interest.

ANATOMY AND EMBRYOLOGY

There is a paucity of new work with reference to the anatomy and embryology of the cornea and sclera in the recent literature (1949-1950); that which has appeared deals chiefly with corneal innervation. Rodger,[1] in reporting his investigation of the pattern of corneal innervation in rabbits, states that he had found three levels of networks formed by the nerve fibers: one in the substantia propria, one under Bowman's membrane and one within the epithelium. Those found in the last structure, end between, and not within, the epithelial cells. From these networks, he differentiates two types of fibers. Data on the innervation of the human cornea are reported by Fornes Peris[2]; he shows by means of photomicrographs that there is no intraepithelial innervation of the cornea. Innervation really terminates in the basal membrane.

Another type of experimental work deals with the so-called Manz glands, which have been identified in swine. Aurell and Kornerup,[3] using the limbal conjunctiva of the newborn and adult of both men and swine, found that these glands in the human being are actually solitary balls of corneal epithelium which have been separated at the limbus from branching ridges of epithelium.

Reasons for classifying stromal cells as reticuloendothelial elements are put forth by Krwawicz,[4] who used rabbits to illustrate his work.

Of statistical importance are the studies of Wilmer and Scammon,[5] who have published tables comparing the growth of the components of the human eyeball in the newborn and the adult. Much of this body of data was compiled from the

1. Rodger, F. C.: The Pattern of Corneal Innervation in Rabbits, Brit. J. Ophth. **34**:107 (Feb.) 1950.

2. Fornes Peris, E.: The Comparative Morphology of the Corneal Fibrocytes, Arch. Soc. oftal. hispano-am. **8**:821, 1948; The Corneal Innervation: Clinical Considerations, ibid. **9**:237, 1949.

3. Aurell, G., and Kornerup, T.: On Glandular Structures at the Corneoscleral Junction in Man and Swine: The So-Called "Manz Glands," Acta ophth. **27**:19, 1949.

4. Krwawicz, T.: The Reticulo-Endothelial System of the Cornea, Brit. J. Ophth. **31**:421 (July) 1947.

5. Wilmer, H. A., and Scammon, R. E.: Growth of the Components of the Human Eyeball: Diagrams, Calculations, Computation and Reference Tables, Arch. Ophth. **43**:599 (April) 1950. Scammon, R. E., and Wilmer, H. A.: Growth of Components of Human Eyeball; Comparison of Calculated Volumes of Eyes of Newborn and of Adults, and Their Components, ibid. **43**:620 (April) 1950.

literature and serves to bring together pertinent facts. According to their summary, the eyeball increases a little less than threefold between birth and maturity. The greatest relative postnatal gain in calculated volume is seen in the iris, ciliary body and choroid. The growth of the lens, retina, anterior chamber, cornea and intrabulbar portion of the optic nerve is distinctly less than that of the eyeball as a whole.

PHYSIOLOGY, PHARMACOLOGY AND EXPERIMENTAL PATHOLOGY

A review of the current literature concerning the physiology, pharmacology and experimental pathology of the cornea reveals that the fortuitous liaison between the ophthalmic clinicians and the workers in the basic sciences is now rapidly bearing fruit. As is to be expected, much of the work is still in a state of flux, and many contradictory findings are reported. Only time and critical coordination of all efforts will eventually clear the haze, so that in the end the "practical" ophthalmologist will have something to "put his teeth into."

That necessity is the mother of invention is well illustrated by the mass of material that has appeared in the wake of keratoplasty concerning the physiology, biochemistry and experimental pathology of the cornea. The demands resulting from surgery of the cornea have forced a reconsideration of this tissue from the point of view of modern physiology and pathology. As a net result, new insight has been gained into pathological pictures, and the possibility of new avenues of therapeutic approach has appeared.

Precorneal Film.—The normal corneal and conjunctival epithelium is constantly bathed and protected by a fluid film. This film, derived from both the lacrimal fluid and secretions of the conjunctival glands, is of a colloid nature. It has a regulated composition, viscosity and wetting potential, so balanced that it remains optically clear. Because of constant contamination by desquamated cellular material, it must be continuously renewed. It is the medium through which gaseous exchange occurs. The film also serves as a diluant and hence protects the epithelium against irritation which might result, even with the commonly employed drug solutions. Any physicochemical change in the component parts of the film influences the health of the epithelium and, if persistent, results in a disturbance (keratitis) of the underlying corneal, stroma. For example, an increase in viscosity owing to an inhibition of lacrimal fluid, as in keratoconjunctivitis sicca, results in a pathological state of the epithelium.

Both the corneal and the conjunctival film lines can be individualized biomicroscopically (with the narrow beam), especially if a solution of fluorescein is instilled, since this substance rapidly diffuses through the film. By this method, gross increases in viscosity resulting from mucus or desquamated material can be seen. Swan [6] has given an excellent résumé of the properties of the precorneal film. He recommends a 0.5 to 1.0 per cent solution of methyl cellulose containing 0.9 per cent sodium chloride as a conjunctival lubricant, cohesive and substitute for the precorneal film. He states that vehicles containing methyl cellulose are better tolerated by the cornea than are simple aqueous solutions because they do not reduce the normal emollient substances of the precorneal film.

6. Swan, K. C.: Pharmacology and Toxicology of the Cornea: Contemporary Concepts, Arch. Ophth. **41**:253 (March) 1949.

Epithelium and Endothelium.—The epithelium and endothelium are the most vital components of the cornea. Physiologically, they guard the integrity of the corneal stroma. The importance of these structures in maintaining the normal health and transparency of the cornea has been well elucidated by Cogan [7] and his associates. It has been shown that to maintain transparency it is essential to keep the cornea relatively dehydrated. Apparently, this partially dehydrated state is not entirely controlled by the osmotic tension, the hydrogen ion concentration of the interstitial fluid or the normal intraocular pressure but, rather, is governed by the permeability properties of the epithelium and endothelium of the cornea. The intact epithelium and endothelium act as semipermeable membranes and as such are permeable to water, but not to electrolytes or to nonlipid soluble nonelectrolytes. With the fluid (film) outside the cornea and the aqueous posterior to it both partially hypertonic in relation to the stroma (whose fluid is derived from the limbal blood vessels), a favorable osmotic gradient keeps the stroma in a deturgescent and clear state. The sclera, not having such a dehydrating mechanism, is normally hydrated to its maximum and consequently is opaque. According to Cogan,[7] "if the sclera is artificially dehydrated so that, like the normal cornea, it contains only a fraction of the water capable of being imbibed, it also becomes transparent."

The importance of this concept for the explanation of the mechanism in the production of epithelial edema and bullae is evident. Any condition which produces a reversal of the osmotic gradient leads to an imbibition of fluid. This is especially so when endothelial damage permits filtration of the more hypertonic aqueous into the stroma and, as a consequence, the osmotic tension of the stromal fluid exceeds that of the blood.

Practically, Cogan showed that the epithelium acts as a semipermeable membrane in that a temporary reversal and clearing of epithelial edema are possible by the instillation of a hygroscopic substance such as glycerin. This is of great aid when examination of the deeper structures is obscured by edema or bedewing of the corneal epithelium.

Normally the epithelium is one of the most transparent elements of the cornea. Biomicroscopically, in optical section, this is evidenced by a narrow black space located just behind the relucent film line. When damaged, the epithelium heals without scar tissue formation, regenerating at an astonishing rate. In many instances, exogenous infections (e. g., viruses), which enter through the epithelium, rapidly pass through Bowman's membrane (lamina elastica anterior) and set up a reaction, usually appearing as infiltrates; within hours, the portal of entrance in the epithelium, because of its rapid repair, may no longer be demonstrable, even biomicroscopically. However, regeneration may be impeded by local anesthetics and drugs. Healing of epithelial defects is aided by heat. This may account for the rapid repair that occurs when the eye is kept closed by a bandage. The epithelium rapidly grows in and fills defects, even though the underlying stroma may be damaged to the point of necrosis. But the epithelium over such areas,

7. Cogan, D. G.: Studies on the Clinical Physiology of the Cornea: Interrelationship of Corneal Turgescence, Epithelial Edema, Bullous Keratopathy, and Interstitial Vascularization, Am. J. Ophth. **32**:625 (May) 1949.

as is well known, may remain weak and break down readily and repeatedly, resulting in recurrent erosions. When the underlying damage is severe, intractable bullae may form.

Corneal Stroma.—As pointed out by Swan, unlike the corneal epithelium and endothelium, the metabolic activity in Bowman's membrane and the corneal stroma is relatively low but increases with vascularization and cellular infiltration resulting from inflammation or nutritional disorders. Substances invade and pass through the stroma by diffusion, but their rate of penetration is largely dependent on the relative physical properties of the substance and the vehicle in which it is dissolved. Diffusion ordinarily occurs from the limbal vasculature toward the axial regions of the cornea. Pathologically, edema of the stroma may be very pronounced after invasion of blood vessels (e. g., interstitial keratitis). Diffusion of substances also occurs through the semipermeable epithelium and endothelium. Damage to these membranes greatly enhances diffusion. For example, it can be readily demonstrated biomicroscopically that if after an abrasion of the corneal epithelium a few drops of fluorescein solution are instilled, a green color can be detected up to the posterior corneal surface within a few minutes. The endothelium is an extremely sensitive membrane, and its permeability is immediately increased by inflammation, trauma, and nutritional and trophic alterations.

The importance that this phase of corneal physiology bears to the pharmacologic problem of the penetration of drugs into and through the cornea is self evident. Many of the older concepts concerning the topical application of drugs have already been disproved. According to Swan, the control of the p_H or the tonicity of vehicles ordinarily used, except for reducing their irritating action, is not as important for the penetration of drugs into the cornea as are the relative physical properties of the drug and the vehicle. A drug should be given in a vehicle for which it has less affinity than for the cornea and conjunctival epithelium. This means that highly water-soluble drugs should be used in an oil vehicle, while highly oil-soluble ones should be administered in water. Although permitting longer contact, ointments and oily solutions do not mix readily with the corneal film. As previously mentioned, a 2 per cent solution of methyl cellulose is a highly effective vehicle for suspensions of water-insoluble drugs. Such a vehicle not only mixes better with the precorneal film but also tends to increase epithelial permeability and, consequently, the effectiveness of the contained drugs.

In cases of emergency, when high and rapid penetration of therapeutic agents is desired, iontophoresis can be employed. Antibiotics and other substances capable of ionization can be forced into and through the cornea. According to Dyson,[8] iontophoresis increases the permeability of the epithelium of the excised cornea to magnesium chloride and levulose, and this alteration in epithelial permeability is of major importance in obtaining high intraocular levels. Von Sallmann also showed that high amounts of alkaloids (atropine and scopolamine), as well as sulfonamides and penicillin, can be introduced into the anterior chamber by this method. This form of treatment has to be carefully controlled because of possible damage to corneal epithelium and the underlying stroma. I have seen a case in

8. Dyson, C.: Influence of Iontophoresis on the Permeability of the Excised Cornea, Arch. Ophth. **42**:416 (Oct.) 1949.

which, owing either to overtreatment or to rough handling, necrosis resulted, with an ensuing dense corneal scar.

Corneal Vascularization.—In his paper on clinical physiology of the cornea,[7] Cogan describes new concepts of corneal vascularization. It seems that when the corneal stroma adjacent to preexisting vessels swells and becomes soft, a lowering of the extravascular pressure results in factors favorable to dilation of vessels. Saccular aneurysms form, which ultimately burst, and as a consequence the hemorrhagic zone becomes infiltrated with new capillaries. These capillaries eventually resolve into infiltrating loops. Lesions confined to the axial, or central, part of the cornea, e. g., herpes or certain dystrophies (keratitis guttata), do not readily become vascularized because they are surrounded by a ring of rigid stroma, and hence there is no stimulus directed to the existing limbal vessels. Cogan postulates that the swelling of the peripheral cornea induces neovasculogenesis, which, in turn, reduces the swelling. This self-corrective cycle results from the fact that with neovascularization the stroma becomes isosmotic with the blood, and therefore hypotonic. Then the process of deturgescence can be resumed (through the action of the hypertonic tear film or aqueous), and the edema (bedewing and bullae) subsides. This can occur in spite of persistent damage to the endothelium, provided more water is abstracted anteriorly (film) than enters the stroma posteriorly or from the blood vessels. Finally, this concept suggests that, in spite of the opacification which always accompanies it, interstitial vascularization of the cornea is beneficent and should be encouraged.

Campbell and Michaelson,[9] employing experimental animals, produced standard corneal lesions. They showed that if a particular lesion is more than a certain critical distance from the limbus no vascularization of the cornea occurs. If a series of "standard lesions" are placed at different distances from the limbus, but within the critical distance, vascularization follows. The distances between the sites of the lesions and the basal angles of the resulting triangular vascular areas are fairly constant. The results suggest that the formation of new vessels in the cornea involves a factor released by the lesion which diffuses from its site.

Stern [10] reported a case of traumatic superficial keratitis in a man having a proved riboflavin deficiency. The cornea had extensive opacities and was highly vascularized. Specific riboflavin therapy resulted in dramatic improvement. It seems "that chronic riboflavin deficiency may produce corneal vascularization only if and when the cornea is exposed to a traumatic factor—be it accidental injury, surgical intervention, chronic mechanical or solar irritation or an allergic reaction." When the cornea is normal, a degree of riboflavin deficiency may remain subclinical or morphologically unrecognizable, but when the cornea is injured, more oxygen, and hence more riboflavin (respiratory enzyme), is required. This may serve to clarify the doubt held by many investigators whether in man ariboflavinosis is attended by corneal vascularization. Evidently, certain pathological states increase the rate of corneal metabolism, and as a consequence vascularization will follow

9. Campbell, F. W., and Michaelson, I. C.: Blood-Vessel Formation in the Cornea, Brit. J. Ophth. **33**:248 (April) 1949.

10. Stern, H. J.: Conditioned Corneal Vascularity in Riboflavin Deficiency: Report of a Case, Arch. Ophth. **42**:438 (Oct.) 1949.

in order to relieve the respiratory deficit. According to Katsnelson,[11] lack of riboflavin causes disturbances of the corneal epithelium and an increase in the marginal loop vessels. He also showed that keratomalacia due to avitaminosis A in the mother is seen in the infant, who may be born with dense opacities of the cornea. The clinical picture varies in adults and in infants. It appears early in infants and late in adults. Both eyes are usually involved in children, as is not always true of adults. This corneal condition may occur in diabetes, thyrotoxicosis, trachoma and tuberculosis of the eye. He claims that thiamine insufficiency causes a disciform keratitis.

Unquestionably, there are many gaps in our knowledge of the effects of vitamin deficiency on corneal metabolism. Until a more thorough understanding of the principles of its physiological processes are available, no definite conclusions can be drawn.

As previously mentioned, the problems arising from modern surgery of the cornea have stimulated considerable thought concerning the vitality and healing processes of its layers. As pointed out by Buschke,[12] the pathologist is no longer satisfied with recording and classifying final histological pictures; rather, the trend is toward dynamic interpretations of the mechanisms leading to morphological changes. This involves a closer relation between pathology and physiology. With this in mind, Buschke first studied the cellular damage following appropriate doses of ultraviolet radiation and the use of mustard gas (2-chloroethyl sulfide) and related substances and, secondly, the healing processes in epithelial wounds. The damage resulting to the epithelium was characterized by the appearance of nuclear fragmentation within several hours and eventually of cell disintegration. It was found that temperature had a profound effect even with damage due to ultraviolet rays, in which no clinical agent was added which conceivably might require a higher temperature in order to react with elements of the tissue. Pathological changes developed after four to six hours at a temperature of 38 C. while morphological integrity was retained for a much longer time at lower temperatures (e. g., 10 C.). Therefore he postulated that metabolic processes within the tissue itself are responsible for the cellular damage. The exact nature and behavior of these metabolic processes are not known, but it seems that enzymes which undoubtedly play a large role in the intrinsic metabolism of the cell are involved. It was also found in some instances that aerobiosis was necessary for the appearance of nuclear fragmentation.

Another example of the dynamic aspects of tissue structure was seen in the healing of epithelial wounds. There was a different morphological response to pinprick injuries than to larger lesions. With the pinprick injuries the most severely damaged cells became separated during the period between injury and onset of cell orientation, forming a sequestrum, which was sloughed off. The adjoining cells were oriented according to the layer in which they were located. The superficial cells were grouped tangentially, forming a microscopically continuous surface. Basal cells were arranged radially and showed pseudopodial extensions.

11. Katsnelson, A. B.: Role of Vitamin Deficiency in the Pathology of the Cornea, Vestnik oftal. (no. 6) **26**:3, 1947.

12. Buschke, W.: (*a*) Some Dynamic Aspects of Tissue Structure in Corneal Epithelium, Am. J. Ophth. **33**:39 (March, pt. 2) 1950; (*b*) Morphologic Changes in Cells of Corneal Epithelium in Wound Healing, Arch. Ophth. **41**:306 (March) 1949.

After two or three hours, the pseudopods of neighboring cells made contact, thus resembling the normal epithelial continuity. With linear and larger injuries, there was a different morphological response. After a latent period, the wound margins became smooth and often assumed an arcade-like shape, owing to a mushroom-like spreading and flattening of the marginal cells. These sealed off the epithelial sheet with a microscopically more or less continuous surface toward the denuded area. Pseudopods were first seen chiefly in places where the wound margin showed smaller pockets. At present, no explanation of these differences is available. It is possible that certain intrinsic properties of the epithelium are responsible.

A study of the variables that might interfere with these cell movements showed that this process depends on an increased temperature and can be interfered with by anaerobiosis and by cyanide, iodacetate and other sulfhydryl-binding substances, as well as local anesthetics.

In addition, the importance of intercellular cohesion was indicated as a variable affecting cell movement. Intrinsic proteolytic enzymes play a role in the interference with cell cohesion. Normally, certain restraining influences must be present to prevent their action. Buschke stated:

> The observations to date, however, appear to be compatible with the idea that processes of breakdown and resynthesis of proteins concerned in intercellular cohesion play some role and that factors regulating the extent of these two opposite phenomena of tissue metabolism may be responsible for physiologic and pathologic variations in cell cohesion.[12a]

Practically, from the further development of such work, we may soon have a firmer basis on which to direct our therapeutic measures; e. g., the time at which to apply different grades of temperature—perhaps cold in the first few hours, to inhibit epithelial damage, and then heat, to stimulate epithelial repair—and the employment of agents for the control of the enzyme action so important to processes of cellular cohesion.

In a similar way, work has been started from the dynamic point of view on the stromal cells of the cornea. This work is of great importance because a better understanding of the method and nature of regeneration of corneal stromal cells is essential in corneal surgery. Friedenwald [13] published a note on the karyolysis of the corneal stroma cells. In contrast to the mode of death which occurs among the wandering cells of the corneal stroma, which is by nuclear fragmentation, death of the stroma cells proper is caused by a process of swelling, followed by bursting of the cell nuclei (these cells are sometimes called corneal corpuscles, or keratocytes). When there is an adequate dose of mustard gas or nitrogen mustard (methyl-*bis* or *tris*[2-chloroethyl] amine), the stroma cell nuclei swell, become pale staining, with margination of the chromatin, and eventually burst. This occurs only when the level of dosage causes easily recognizable clouding of the cornea, and permanent scarring of the cornea often results. The same type of death is seen with the use of arsenicals, alkali burns and freezing.

This phenomenon can also be observed in stroma cells of enucleated eyes kept in a moist chamber in the incubator. Thus, the infiltration of inflammatory cells is eliminated when the cornea alone is stored; there is no swelling or bursting. There is a repetition of this effect when isotonic sodium chloride solution is used.

13. Friedenwald, J. S.: Studies on Physiology, Biochemistry, and Cytopathology of Cornea in Relation to Injury by Mustard Gas and Allied Toxic Agents: Note on Karyolysis of the Corneal Stroma Cells, Bull. John Hopkins Hosp. **82**:178 (Feb.) 1948.

Since the process occurs in vivo and in the whole enucleated eye, but not in the isolated stored cornea, it is assumed that the ocular tissues or fluids provide a factor, probably a metabolite, which is responsible for this pathological process. Pyknosis will also occur with a sufficiently large dose.

Duane [14] has compiled a valuable summary of the various problems associated with corneal metabolism. He points out that the question is still unsolved as to whether the cornea uniquely procures oxygen directly from the atmosphere, as distinguished from other tissues, which are supplied exclusively by oxygen borne in the blood stream. Likewise, little is known regarding metabolism in the various corneal strata, especially the metabolism concerned with respiratory enzymes. Duane stresses the importance of continued study in these fields and emphasizes that until more positive data are accumulated one cannot hope to understand pathological processes in the cornea.

In an interesting paper on the mechanism of corneal wound healing, Hoffman and Messier [15] first studied the cells involved in corneal growth and repair and then the behavior of recipient and donor cells in grafts. Rabbit cornea was preserved in vitro indefinitely. In vitro a pattern of growth of stromal cells was observed. This pattern includes a latent period before growth begins and a noticeable reversibility in the form of stromal cells in response to environmental changes (especially changes in temperature). Irradiation with a low dose shortens the latent period, and growth can be increased by the addition of aqueous sheep heart extract. The cells obtained on culture of corneal tissue exhibit fibrocytic characteristics. Stromal cells are not specific for the cornea but may be derived from adjacent fibrous structures, and they then conform to the form of stromal cells.

Experiments on the behavior of recipient and donor cells led to the following observations:

1. Corneal grafts made with donor material grown in tissue culture before operation caused a marked repellent reaction of the recipient cornea to all attempts of the donor cells to grow into the recipient cornea.

2. Corneal grafts made with frozen material resulted in healing of the edges but with necrosis and scarring of the center of the graft.

3. Freezing experiments showed that normal stromal cells can migrate into a devitalized area and take up the normal metabolism of this area provided that passage across the wound edges is not delayed too long.

4. Growth extract did not accelerate this passage when frozen donor material was used, and necrosis and scarring occurred before it had been accomplished.

Evidently, the cells in the donor cornea play no part in the healing of a corneal graft; this function belongs to the recipient cornea.

When devitalized material is used, the maintenance of transparency of the graft depends on the rapid passage of recipient cells into the donor tissue. With fresh material, the viable cells are capable of carrying on metabolism until they are

14. Duane, T. D.: Metabolism of the Cornea, Arch. Ophth. **41**:736 (June) 1949.

15. Hoffman, R. S., and Messier, P. E.: Mechanism of Corneal Wound Healing: I. Cells Involved in Corneal Growth and Repair, Arch. Ophth. **42**:140 (Aug.) 1949. Messier, P. E., and Hoffman, R. S.: Mechanism of Corneal Graft Healing: Behavior of Recipient and Donor Cells, ibid. **42**:148 (Aug.) 1949.

replaced by the cells of the recipient cornea. Hence it is felt that a corneal graft heals more like a bone or preserved cartilage graft than like a "free" skin graft; consequently, corneal grafts should be considered a replacement type.

Further work along these lines was done by Maumenee and Kornblueth.[16] They found that the rabbit cornea will regain its normal clinical and histological appearance after most, if not all, of the stromal cells have been destroyed by freezing, that the stromal cells die by nuclear fragmentation after freezing and that destroyed stromal cells are replaced by migration and multiplication of undamaged corneal corpuscles and by transformation of wandering macrophages. Choyce[16a] pointed out that Maumenee and Kornblueth had not proved conclusively that their freezing technic killed any considerable number of stromal cells and that their work sheds little light on the vexing question of the "fate of the graft," since ordinarily donor material is not subjected to a temperature of —78 C. before use.

To determine the best method of preserving corneal transplants, Sédan Bauby, Sédan and Payan[17] studied four series of enucleated eyes of dogs. In eyes preserved in ice with humid air 24 hours after death massive desquamation of the epithelium with bullae developed on the fifth day. In eyes preserved similarly immediately after death the same changes took place in nine days. When the eyes were preserved in citrated autoblood, necrosis of the lamina basalis was seen on the ninth day. In the fourth series liquid petrolatum was used; bullae were seen on the seventh day. The anterior epithelium was least destroyed when the enucleated eyes were placed immediately in liquid petrolatum.

In his review of the ultimate fate of the graft, Katzin[18] brings out some pertinent material. He points out that the closer the relationship between the donor and the recipient, all other factors being equal, the better is the chance for a successful "take." This was well demonstrated in small experimental animals by the fact that when tissues were transplanted from one species to another grafts were not accepted. Undifferentiated tissues of low vitality lend themselves to grafting better than do those not so constituted. The cornea, like cartilage and perichondrium, is favorable because of its relatively low nutritional requirements, its large proportion of intercellular matrix and its low vascularity or absence of blood supply. In regard to the fate of the various layer components of the transplanted cornea, it appears that "the donor cornea is a framework which the host's cornea gradually fills in with its own cellular elements while maintaining the original matrix.[11] Although both epithelium and endothelium of the graft are probably replaced, Bowman's membrane of the graft persists. Since Bowman's membrane does not regenerate, defects within it are filled in part either by epithelium or by fibrous tissue or by both. Clinically, this also occurs in the healing of ulcers. Ordinarily Descemet's membrane (lamina elastica posterior) tends to remain intact. However, it is known that it can regenerate if damaged. The noncellular

16. Maumenee, A. E., and Kornblueth, W.: Regeneration of the Corneal Stroma Cells: II. Review of the Literature and Histologic Study, Am. J. Ophth. **32**:1051 (Aug.) 1949.

16a. Choyce, D. P.: Maumenee and Kornblueth,[16] abstracted, Ophth. Lit. **3**:2686, 1950. on Experimental Lesions of the Cornea, Boll. Soc. ital. biol. sper. **25**:260 (March) 1949.

17. Sédan Bauby, S.; Sédan, J., and Payan, H.: Function of the Preservative on Histological Changes of Corneas Kept in the Ice Box After Keratoplasty, Ann. d'ocul. **182**:364 (May) 1949.

18. Katzin, H. M.: The Ultimate Fate of the Graft, Am. J. Ophth. **33**:35 (March, pt. 2) 1950.

elements (matrix) of the stroma remain, but if it is to remain clear a rapid replacement of the more delicate cells must occur. This means that the host's stroma must contain a sufficient number of normal stromal cells.

Experimental studies of nerve changes in the rabbit cornea after transplantation were reported by Escapini.[19] The corneal nerves behave like any peripheral nerve after severance, showing regressive changes, followed by regenerative ones. In transplantation there are regressive changes in both host and graft (wallerian degeneration). Reinnervation occurs by formation of nerve fibers which grow from the nerves of the host around the graft. Physiological tests elicit a respone 45 days after operation; this response increases but never reaches normal.

De Berardinis and Bonavolontà[20] studied the amino acids (cysteine, proline, asparagine, glutamine, histidine, arginine and tryptophan) for their cicatrizing activity on experimental corneal lesions. Ordinarily (in control animals) the average time of cicatrization was 96 hours. Corneal wounds treated with a single amino acid healed in from 44 to 72 hours. Arginine and histidine were particularly effective. Similarly, de Vincentiis[21] found that norvaline (α-aminovaleric acid) accelerated cicatrization of experimental corneal wounds.

Sclera.—As yet, considerably less work has appeared on the physiology and experimental pathology of the sclera. Undoubtedly, with the increase in scleral surgery and the advent of new hormonal therapeutics, many questions regarding physiology and pathology of the sclera will have to be answered. Swan[22] points out that the sclera is composed of interlacing collagenous fibers, with only occasional fine elastic fibers, few vessels and an amorphous ground substance. There is a relative paucity of cells as compared with some other types of connective tissue. With this in mind, it is evident that the response to insult, inflammation or injury will in part be governed by potentials inherent in and peculiar to such a tissue. Proliferative reactions cannot be as marked as in other tissues and will occur chiefly by invasion of cells from adjacent tissue or by penetration of vessels into the sclera. In other cases the response will be primarily a physicochemical one, such as hyalinization. Unlike the deturgescent cornea, where wounds heal by primary intention, with relatively little contraction (clean injuries), scleral fibers do not swell easily but, rather, tend to retract, and the gap has to be filled in with proliferated tissue from neighboring sources (episclera and choroid), with the later laying down of collagen. Hence healing occurs by secondary intention. As a result, anteriorly, after cataract incisions, if the section extends into the sclera, a "fibroplastic ingrowth" may invade the anterior chamber and simulate epithelial downgrowth. In the absence of an active inflammatory reaction, fibroplastic ingrowth in the anterior chamber is self limited in most instances, but if adhesions to the iris or vitreous occur, the process may eventuate in secondary glaucoma, or even retinal separation. Posteriorly, after sclerotomy or operation for retinal separation, fibroplastic ingrowth may be fortuitous in causing a fusion of the retina

19. Escapini, H.: Degeneration and Regeneration of Nerves in Corneal Transplantation: Experimental Study, Arch. Ophth. **39**:135 (Feb.) 1948.

20. de Berardinis, E., and Bonavolontà, G.: Cicatrizing Activity of Various Amino Acids on Experimental Lesions of the Cornea, Boll. Soc. ital. biol. sper. **25**:260 (March) 1949.

21. de Vincentiis, M.: Cicatrizing Effect of α-Amino-Valeric Acid on Experimental Wounds of the Cornea, Boll. Soc. ital. biol. sper. **25**:265 (March) 1949.

22. Swan, K.: Some Contemporary Concepts of Scleral Disease, to be published.

with the choroid and sclera, provided there is no penetration into the vitreous. Fibroplastic invasion into the vitreous with subsequent contraction has dire results. Dependent on the type of cellular infiltration, whether leukocytic or lymphocytic (chronic inflammatory cells), inflammatory reactions of the sclera may be divided into suppurative and granulomatous. Rarely, suppurative reactions (abscess formation) may follow direct inoculation of bacteria into scleral wounds or indirect invasion of the sclera by pyogenic processes in adjacent tissue. More commonly, such scleral lesions are associated with metastatic lesions elsewhere. The clinical diagnosis of granulomatous scleritis may be difficult but should be suspected in all cases of low grade, recalcitrant uveitis of the anterior segment. As a consequence of inflammation, loss of scleral substance results in thinning of this tissue, which clinically is demonstrable by the presence of typical bluish areas, where the underlying pigmented zones show through. It is known that subconjunctival injections of medicaments may result in granulomatous scleritis. Hypersensitivity may also play a role in such reactions. Lately there has been a great deal of renewed interest in hypersensitivity responses occurring in the so-called collagen tissues, e. g., dermis of the skin, walls of blood vessels, synovial membranes or sclera. Some of the types of diffuse localized or nodular episcleritis may be manifestations of diffuse collagen disease. Clinically the scleral reaction in this condition may be marked by the associated uveitis, or it may be abortive. Swan feels that scleromalacia perforans, which may occur in association with arthritis, fits into the group of disseminated collagen diseases. In addition to the scleral involvement, there is atrophy of the subepithelial connective tissue of the conjunctiva of Tenon's capsule and about the extraocular muscles. Histologically it was observed that focal areas of fragmentation of collagen fibers and granular clumping of the ground substance of the sclera resembled the "fibrinoid degeneration" of collagen seen elsewhere in these conditions.

Among the conditions affecting the sclera are some which are not associated with any appreciable amount of cellular or vascular response. A common one is the so-called hyaline plaque, which is not infrequently seen in older persons. A high percentage of persons demonstrating these plaques, which are usually vertically oval and located in front of the insertion of the rectus muscles, had signs of osteoarthritis.

DISEASES OF THE CORNEA AND THEIR TREATMENT

The cornea has always been the object of great interest to ophthalmologists, and with the introduction of new drugs [23] and new methods of therapy into the field of medicine this interest has received new stimulation. Reports of experiments have been numerous. Only conditions which have appeared frequently in recent literature will be discussed.

Keratoconjunctivitis Sicca.—Keratoconjunctivitis sicca is one of the conditions to be included, since the cornea is more involved than the conjunctiva. Henderson [24] recently reviewed the disease and added 121 cases to those already recorded in the literature.

23. Already, reports concerning the favorable effects of hormone therapy (cortisone and ACTH) are filtering through. At present, insufficient data preclude any worth while critical evaluation of this form of therapy.

24. Henderson, J. W.: Keratoconjunctivitis Sicca: Review with Survey of 121 Additional Cases, Am. J. Ophth. **33**:197 (Feb.) 1950.

Various systemic manifestations have been found so constantly associated with keratoconjunctivitis sicca that together they constitute Sjögren's syndrome. These are dry mouth, dry nose, dry throat, hoarseness and intermittent enlargement of the parotid glands, and in Henderson's series of 121 cases, the most recent published, these associated symptoms were present in at least 33 per cent. Xerostomia is the most frequently observed of these symptoms, indicating involvement of the salivary glands. Its relation to arthritis is still not clear.

Therapy at this time is chiefly symptomatic, since no definite etiologic factor has been established. Vitamins, hormones, various measures to improve the general health and even bilateral section of the vertebral nerves and bilateral resection of a part of the superstellate segment of the cervical sympathetic chain have been tried. At present, the best available means is replacement therapy or use of artificial tears. One may use collyriums, water and methyl cellulose. In any case, the patient's response is the test, as there are no uniform results from any type of treatment. The solution which alleviates his symptoms is the method of choice. As yet, no reports are available as to whether treatment with cortisone (17-hydroxy-11-dehydrocorticosterone) or ACTH (pituitary adrenocorticotropic hormone) is beneficial.

Ulcerative Keratitis.—Dendritic ulcer is a condition which presents a definite pathological picture. In the latter part of 1949, Klein and Miller [25] reported the results of their experiments using hypertonic solutions (25 per cent of urea). They applied these solutions locally in an eye bath and found that healing of dendritic and marginal ulcers was favorably influenced. To have any effect, the solutions used must be sterile and fresh. Breakdown of the healed cornea was prevented by the use of a mild lubricating ointment. Aureomycin has recently replaced other drugs as the treatment of choice. This drug is applied topically (O'Gonner) as a 0.5 per cent solution, 1 drop being instilled into the conjunctival sac every one or two hours during the day. Symptoms are rapidly relieved, even before epithelization is complete, and the duration of medication is directly proportional to the size of the ulcer. Previously, Gifford's iodine solution [26] was used, but the results of this are quite unsatisfactory as compared with those of the aureomycin. Roentgen therapy has also been tried with promising reports.

Another frequently diagnosed lesion is the serpiginous ulcer of Mooren. Linn [27] states that this ulcer shows so many of the characteristics of virus infections that it should properly be classified with them. Many kinds of therapy have been tried, without much success; these include chemical agents, physical agents, paracentesis, formation of a conjunctival flap, chemotherapy and use of the early antibiotics. Stein [28] reports good results from his series of 16 cases of serpiginous ulcer which

25. Klein, M., and Miller, S. J. H.: Local Application of Urea for Treatment of Dendritic Ulcer, Brit. J. Ophth. **33**:643 (Oct.) 1949.

26. A saturated solution of iodine made by adding 5 minims (0.3 cc.) each of tincture of iodine and glycerin to 10 grains (0.65 Gm.) of powdered iodine crystals with 3 drops of saturated potassium iodide solution.

27. Linn, J. G.: Chronic Serpiginous Ulcer of the Cornea (Mooren's Ulcer): Etiologic and Therapeutic Considerations, Am. J. Ophth. **32**:691 (May) 1949.

28. Stein, A.: Contribution to Treatment of Corneal Ulceration, Particularly Serpiginous Ulcer, Arch. d'opht. **9**:722, 1949.

he treated with penicillin administered by iontophoresis and a continuous corneal bath. He used a special eye cup of plastic containing an electrode and rimmed with a rubber sleeve. It was held in place by a wide elastic band passed around the head. The penicillin was used in a concentration of 20,000 units in 10 cc. of distilled water, and iontophoresis was applied in half-hour periods twice daily until the disappearance of the infiltration. The amount of current varied from 0.75 to 2.0 milliamperes, depending on the tolerance of the patient. Between these periods, the eyes were bathed in a penicillin bath of from 20,000 to 40,000 units in an artificial tear solution; this therapy was continued from six to eight hours. Recently, Braley and Sanders [29] tried local treatment with aureomycin borate in a 0.5 to 1.0 per cent solution; the results show promise for a quick and efficient method of treating this ulcer.

Another form of ulcer which may invade the cornea is the "catarrhal," or marginal ulcer. The best results in the treatment of this condition were obtained by combined injections of penicillin into the anterior chamber and into the conjunctiva. Sulfonamides seem to be ineffective. Theodore [30] recommends a 5 per cent solution of sodium propionate for catarrhal ulcers, especially those from which coagulase-positive Staphylococcus aureus is isolated.

Gallenga and Rossi [31] used plesiotherapy in their cases of herpes simplex, with apparently beneficial effects. Injections of placental extract were used, as well as injections of bee venom; these also were reported to produce the desired effect. The newest work to appear this year was on the use of aureomycin borate (local application). Thygeson and Hogan [32] treated 24 patients; at least 60 per cent of any group, they feel, can be expected to respond with healing in four to seven days, depending on the severity of involvement before treatment is started. In all their cases aureomycin borate (0.5 per cent) was instilled locally. Each patient was given freshly prepared solution to use in the affected eye every half-hour, day and night, for 48 hours, after which he was given a fresh solution. The authors feel, however, that the old method of applying iodine can give equally good results and perhaps will supplement the use of aureomycin. Iodine should be used if the lesion fails to respond within a reasonable period. The use of roentgen rays has lately become popular for treating herpetic lesions. The usual course of therapy is five to six applications of 60 to 80 r at five to six day intervals. The proponents of this method urge that it be used more frequently, even for less severe diseases. Dennie, Morgan and Coombs [33] recommend moccasin venom for the treatment of herpes zoster. Corneal involvement was rapidly checked in two cases and was probably prevented in two others. The venom was given intradermally. Atropine,

29. Braley, A. E., and Sanders, M.: Aureomycin in Ocular Infections: Preliminary Report, J. A. M. A. **138**:426 (Oct. 9) 1948.

30. Theodore, F. J.: Use of Propionates in Ophthalmology: A Preliminary Report, Arch. Ophth. **41**:83 (Jan.) 1949.

31. Gallenga, R., and Rossi, A.: Results of Plesiotherapy for Corneal Diseases, Rassegna ital. d'ottal. **15**:7 (Jan.-Feb.) 1946.

32. Thygeson, P., and Hogan, M. J.: Aureomycin in the Treatment of Herpes Simplex Corneae: Preliminary Report, Am. J. Ophth. **33**:958 (June) 1950.

33. Dennie, C. C.; Morgan, D. B., and Coombs, F. P.: Treatment of Herpes Zoster with Moccasin Venom, J. Invest. Dermat. **12**:153 (March) 1949.

antibiotics (chiefly aureomycin) and supportive measures were employed. Immune serum, if available, can be used also, in doses of 250 to 450 cc. of blood. Roentgen therapy may also be beneficial.

Blatt [34] reports favorable results with penicillin injected into the anterior chamber; the dose varied from 500 to 1,000 units, administered every six hours. Failure was noted when the usual routes were used. Weskamp [35] performed keratectomy in five patients with syphilitic interstitial keratitis at various stages of the disease and reported on the histopathological alterations. Chronologically, the changes observed were (1) the infiltrative and edematous stage, (2) cellular necrosis and vascularization, (3) atrophy of the parenchyma and (4) organization of fibrous tissue.

Corneal Dystrophies.—Dystrophies of the cornea constitute a large group of degenerative lesions of the cornea; the process starts as a mild nutritional disturbance and progresses through stages of tissue degeneration. There are many classifications of these, all of which serve simply to confuse the reader. Goar [36] has classified them as follows to help in eliminating confusion:

1. Fatty, or lipid, degeneration
2. Marginal dystrophy
3. Band-shaped or zonular dystrophy
4. Nodular dystrophy of Salzmann
5. Familial and hereditary forms
   (*a*) Granular
   (*b*) Macular } Buckler's classification
   (*c*) Reticular
6. Endothelial and epithelial dystrophy

Other entities could be included, such as arcus senilis and cornea farinata of the aged.

Treatment of the hereditary dystrophies is without success except in cases that are suitable for corneal transplantation. Lately encouraging reports are available. Roberts [37] cites 100 per cent success in 8 cases of hereditary dystrophy treated by means of penetrating corneal grafts. However, in three cases of Fuchs's dystrophy none of the grafts remained clear. Roberts does not identify the forms or types of dystrophy in his eight cases. If these were familial dystrophies, his report is at variance with the results given by others who have used penetrating corneal grafts in such cases.

Riboflavin Deficiency.—When Bessy and Wolbach maintained rats on a riboflavin-free diet, corneal vascularization resulted. Corneal vascularity is a condition in which newly formed blood vessels leave the limbal plexus and enter the sub-

34. Blatt, N.: Intraocular Therapy with Penicillin in Syphilitic Infections of the Eye, Arch. d'opht. **10**:62, 1950.

35. Weskamp, C.: Histopathology of Interstitial Keratitis, Am. J. Ophth. **32**:793 (June, pt. 1) 1949.

36. Goar, E. L.: Dystrophies of the Cornea, Am. J. Ophth. **33**:674 (May) 1950.

37. Roberts, J. E.: Statistics on Results of Keratoplasty, Am. J. Ophth. **33**:21 (March, pt. 2) 1950.

epithelial space of the true cornea in a centripetal manner.[38] The limbus is about 1 mm. wide and is composed of the scleral edge, which overlaps the corneal tissue; there are many blood vessels in this area, usually empty. These vessels respond quickly to any irritant by becoming engorged. Most ophthalmologists believe that filling of the limbal plexus, injection of the circumcorneal area and engorgement of the limbus constitute prodromal signs of riboflavin deficiency; they are actually nonspecific, suggestive signs. An advanced case of riboflavin deficiency will show new vessels throughout the entire circumference of the cornea; it is usually bilateral.

This syndrome must be differentiated from various conditions which in themselves give rise to vascularity of the cornea; these are rosacea keratitis, phlyctenular keratitis and trachoma. In rosacea keratitis there is formation of vessels in the upper quadrants of the cornea chiefly. This area shows subepithelial infiltrates, which increase in size and progress toward the center and the deeper layers of the stroma. Eventually, there are ulceration and fascicular vascularization, the latter differing from that of ariboflavinosis.

Phlyctenular keratitis also causes vascularization of the cornea. It has been shown that this disease is really a state caused by a combination of allergy [39] and riboflavin deficiency. It responds to riboflavin therapy. Roentgen radiation used in a dose of five to six applications of 60 to 80 r at five to six day intervals has been found useful in the therapy of this lesion.

Occasionally, healed trachoma displays an unusual activity which responds to riboflavin therapy; this implies an exacerbation, owing to a lack of the vitamins. Deficiency in any one or more of the essential amino acids causes the same type of vascularity as does lack of riboflavin. These substances are necessary to the normal metabolism of the cornea. A lesion of this type can be precipitated by any conditioning factor, such as mechanical or chemical trauma, so long as there is a subnormal amount of riboflavin in the tissues. A therapeutic test makes possible the final diagnosis. Riboflavin is given in doses of 5 to 15 mg. per day as an adjunct to the diet.

Epidemic Keratoconjunctivitis.—Epidemic keratoconjunctivitis is a relatively new disease in the United States. It has been shown to be caused by a filtrable virus. Thygeson [40] believes that this virus is so easily transmitted because it survives drying and dilution well. Transmission occurs by the use of contaminated tonometers, contaminated solutions and contaminated fingers (those of the physician).

The disease begins as acute follicular conjunctivitis with edema of the lids and transient membranes. There is a scanty secretion, containing almost entirely mononuclear cells. About 10 days later the cornea shows involvement, in one of two forms, erosive or nodular. The punctate lesions are subepithelial and occur together in groups in the pupillary area with subsequent diminution of vision. The inflammatory process usually subsides spontaneously; scar tissue replaces the corneal infiltrates. Active therapy has been directed toward prevention of corneal

38. Stern, J. J.: The Ocular Manifestations of Riboflavin Deficiency, Am. J. Ophth. **33**:1127 (July) 1950.

39. Woods, A. C.: Ocular Allergy, Am. J. Ophth. **33**:1457 (Nov.) 1949.

40. Thygeson, P.: The Epidemiology of Epidemic Keratoconjunctivitis, Am. J. Ophth. **32**:951 (July) 1949.

complications. Prophylaxis should be practiced. When streptomycin was first introduced, it was found to be effective in decreasing the duration of the lesion; it is given in doses of 0.8 to 6.0 Gm. daily. Aureomycin borate is now being used locally in 0.5 to 1.0 per cent solutions, with excellent results. Convalescent serum may also be utilized. In 1948-1949 several epidemics broke out in France.[41] Lépine, Levaditi, Barski and Plessier[41h] performed preliminary experiments on epidemic keratoconjunctivitis with the following results: 1. The condition developed in four of eight monkeys inoculated. 2. The virus could not be isolated. 3. The virus could be cultivated in Maitland's medium. 4. From only one of the affected monkeys was it possible to transmit the virus to mice so as to produce the typical cerebral lesions. 5. No transmission was possible with rabbits and dogs. 6. No typical histological or bacteriologic clue was seen in conjunctival scrapings viewed with the ordinary microscope. 7. In one case, with the electron microscope, certain round corpuscles were seen, which may prove to be important.

Leprosy.—Leprosy is not commonly seen in ophthalmologic practice in this country. A fairly large amount of work, however, has appeared in the past two years on this disease. The usual ocular complication is keratitis, which varies from a micropunctate form to complete clouding of the cornea with dense precipitation, the degree of involvement depending on the duration of the systemic disease. In children, it has been found to occur first as beading of the corneal nerves, followed by punctate keratitis, which gradually develops into interstitial keratitis, greatly resembling that of congenital syphilis. Before the advent of aureomycin, treatment was symptomatic and consisted of irrigations and cleansing of the affected parts. In the series presented by Elliott,[42] 30 patients were treated with aureomycin and 20 by the usual methods. An aureomycin hydrochloride solution was instilled twice daily; it was prepared by combining 5 cc. of distilled water, 25 mg. of aureomycin, 25 mg. of sodium borate and 25 mg. of sodium chloride. The solution was freshly made every 48 hours. Slit lamp examination showed improvement of the superficial punctate keratitis and disappearance of the plaques. The deeper, diffused keratitis showed no change. There was also improvement on the corneal surfaces in those cases in which the cornea was almost completely opaque due to a precipitate type of keratitis throughout the substantia propria.

DISEASES OF THE SCLERA

Only a small amount of material on diseases of the sclera is to be found in the literature of the past two years. Most of it appears as abstracts of articles from foreign journals.

41. (*a*) Gillen, J. J.: Epidemic Keratoconjunctivitis, Concours méd. **71**:861 (April 16) 1949. (*b*) Dubar, J., and Vidal, R.: Evolution of Epidemic Keratitis, Bull. Soc. d'opht. France, March 1949, p. 424. (*c*) Offret, A., and Offret, G.: Outbreak of Epidemic Contagious Conjunctivitis at the Renault Factories at Billancourt, ibid., Feb. 1949, p. 337; (*d*) March 1949, p. 429. (*e*) Vidal, R.: Notes on Epidemic Keratoconjunctivitis, Concours méd. **71**:1068 (May 7) 1949. (*f*) Dollfus, M. A.: Personal Experiences of Epidemic Keratoconjunctivitis, Bull. Soc. d'opht. France, March 1949, p. 425. (*g*) Hartmann, E: Outbreak of Epidemic Keratoconjunctivitis in Neighborhood of Paris, ibid., Feb. 1949, p. 329. (*h*) Lépine, P.; Levaditi, J. C: Barski, G., and Plessier, P.: Early Results of Experimental Research Undertaken in Connection with Epidemic Keratoconjunctivitis: Transmission of the Illness to Monkeys and Mice, ibid., March 1949, p. 419.

42. Elliott, D. C.: Aureomycin in Leprosy, Am. J. Ophth. **33**:1029 (July) 1950.

Tuberculous Scleritis.—Von Herrenschwand [43] reported in detail his method of treating tuberculous scleritis. He advocated percutaneous tuberculin therapy by means of Ektebin ointment, which contains killed tubercle bacilli of both human and bovine strains and a tuberculin. He found the method to be uniformly effective. Tuberculous scleritis usually pursues a torpid, almost painless course with circumscription and destruction of the tubercle and association with chronic anterior uveitis.

Episcleritis.—This condition is often associated with rheumatism or rheumatoid arthritis. Mann and Markson [44] report prompt improvement of symptoms with the use of ACTH. This substance was first given in a dose of 10.0 mg. intramuscularly every eight hours; the amount was then decreased to 20.0 mg. daily, given in three divided doses, and was again decreased to 10.0 mg, daily, administered at 12 hour intervals.

Scleritis.—Atrophy results from this type of lesion with ectasia and staphyloma. The complications are many and serious, leading to keratitis and uveitis. The ectatic area may rupture, with complete loss of vision. Treatment has not proved helpful. Mendoza González and Avales [45] discussed the pathogenesis of inflammatory disorders of the sclera. Harbater [46] reported a case of bilateral scleromalacia perforans. Endophthalmitis developed in the right eye, and enucleation was required. The disease accompanied chronic rheumatoid arthritis of long standing, and in the course of about 20 months, slowly progressed to involve most of the anterior portion of the sclera in a necrotizing process. An unusual feature was associated marginal necrosis of the cornea. This case occurred before hormone (ACTH and cortisone) [47] therapy was available. Perhaps with the employment of these substances in the early stages of collagen tissue involvement the disastrous consequences may be averted.

Senile Plaques.—Senile plaques are often found in the sclera; they are an indication of age and loss of the normal function of the sclera. Sena and Cerboni [48] present their work in a case of senile hyaline plaques and bilateral excavations of the sclera. They discuss the history and pathology of such common disorders of the sclera as senile hyaline plaques, inflammatory processes and scleromalacia perforans. Mitter [49] also presents a case of scleromalacia perforans and discusses scleral degenerations.

Application of Beta Rays.—Beta radiation has become useful in the field of ophthalmology as a therapeutic aid, since it can be limited to superficial tissue or

43. von Herrenschwand, F.: The Treatment of Tuberculous Scleritis, Ophthalmologica **118**:161 (Sept.) 1949.

44 Mann, W. A., and Markson, D. E.: A Case of Recurrent Iritis and Episcleritis on a Rheumatic Basis Treated with ACTH, Am. J. Ophth. **33**:459 (March, pt. 1) 1950.

45. Mendoza González, E., and Avales, G. E.: Pathogenesis of Inflammatory Disorders of the Sclera, An. Soc. méx. de oftal. y oto-rino-laring. **23**:38 (Jan.-March) 1949.

46. Harbater, M.: Scleromalacia Perforans: Report of a Case, Arch. Ophth. **41**:183 (Feb.) 1949.

47. Gordon, D. M., and McLean, J. M.: Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy in Ophthalmic Conditions, J. A. M. A. **142**:1271 (April 22) 1950.

48. Sena, J. A., and Cerboni, F. C.: Scleral Excavations, Arch. oftal. Buenos Aires **23**:313 (Oct) 1948.

49. Mitter, S. N.: Scleral Degenerations: A Case of Scleromalacia Perforans, Brit. J. Ophth. **32**:899 (Dec.) 1948.

surfaces. Its use is based on the production of obliterative endarteritis: The endothelium is the most sensitive part of the vessels. Twenty years ago, beta irradiation was successfully employed in treating pterygiums and hemangiomas of the sclera. Friedell, Thomas and Krohmer [50] describe the Sr^{90} beta ray applicator which they used in a series of cases and discuss the cases in which it was found of value. The following conditions appear favorable for irradiation:

1. Superficial tumors. Small benign tumors, especially papillomas of the lids and conjunctiva, respond well to beta irradiation. Bowen's disease, or intra-epithelial epithelioma, can be destroyed, without deeper damage. Angiomas of the lids and conjunctiva in infants show good results if treated early, including the cosmetic effect. Pterygiums, both new and recurrent, and pingueculae are obliterated by this method. The usual course of therapy was 300 r weekly for a total of 1,200 r.

2. Vernal conjunctivitis. If treatment is given early in the disease, the response is excellent. This is because the papillae then consist of proliferating, young fibrous tissue, new vessels and lymphoid cells, all of which are radiosensitive. In old cases the plaques show hyalinization, which is radioresistant, and these lesions must usually be removed by excision first. The dose is usually 1,200 r.

3. Tuberculosis of the anterior segment. Woods used beta radiation in the treatment of this disease and obtained a favorable response in more than 50 per cent of cases. There is no decrease in the recurrence but a remission in the immediate attack; the mode of action is not known.

4. Vascularization of the cornea. Beta radiation is used both to obliterate and to prevent corneal vascularization. It inhibits the proliferation of capillary endothelium in newly formed vessels, and the progress of invading loops of vessels can be stopped. Even larger and well established vessels can be obliterated if greater amounts are applied. It has been favorable in the following situations:

(*a*) After superficial keratectomy to prevent revascularization of the corneal stroma. The treatment should be started after the first 24 hours and applied at the limbus.

(*b*) Preliminary to corneal transplantation when there are invading vessels in the cornea. Castroviejo used these rays postoperatively; the results are tabulated by Okrainetz.[51] The preoperative vascularization was treated before transplantation at Manhattan Eye and Ear Hospital, with good results. It had been found that clouding of the graft occurred with regularity when there had been preoperative vascularization of the cornea.

(*c*) After corneal transplantation when there is a possibility of vessels invading the graft from the surrounding cornea. There is diversity of opinion as to the wisdom of this procedure; many feel that preoperative irradiation is much more successful.

(*d*) In vascularized corneal leukomas associated with symptoms of irritability, photophobia and lacrimation. Chemical burns of the cornea often show these symptoms and respond gratifyingly to beta irradiation.

50. Friedell, H. L.; Thomas, C. I., and Krohmer, J. S.: Beta-Ray Application to the Eye, Am. J. Ophth. **33**:525 (April) 1950.

51. Okrainetz, C. L.: Beta Irradiation of the Eye Using the Radium-D Applicator, Am. J. Ophth. **33**:52 (March, pt. 2) 1950.

5. Corneal Ulcers. Pyogenic ulcers in the acute stage do not react to this type of therapy; perforation may follow its use. Some types of chronic ulcer heal with radiation therapy applied to the limbal region directly adjacent to the ulceration. There are no contraindications.

The beta rays are beneficial, not in themselves but because of their ionizing radiation and their lack of penetration into the deeper structures.

SURGICAL TREATMENT

During the last 10 years considerable strides have been made in the field of keratoplasty. Much more information is now available concerning indications, contraindications, technic and complications. With selectivity and with better preoperative preparation a higher percentage of successful results will undoubtedly follow. Especially interesting and encouraging is the use of lamellar corneal transplants and radium (for control of vascularization) as therapeutic means. According to Paufique,[52] lamellar keratoplasty has three indications: (1) optical, for superficial lesions; (2) preparatory, for serious lesions (dense and highly vascularized leukomas), with the view to preparing the cornea for a perforating graft, and (3) therapeutic, for progressive corneal diseases. According to Filatov's original observation, as a result of the trophic action of the graft, there seems to be definite improvement (clearing) in the diseased cornea after six or 12 months in an area around the graft. Therapeutic lamellar grafting is a safe operation, and Paufique recommends it for all forms of chronic or recurrent keratitis when ordinary therapy fails, when the center of the cornea is in danger and when corneal perforation is feared. He has obtained good results with herpes, dystrophies, deep syphilitic and tuberculous keratitis and even abscess of the cornea. Together with other necessary procedures, lamellar keratoplasty improves conditions for a subsequent perforating graft. This alone may place many conditions hitherto considered hopeless in the category of operative ones. Apparently, if a lamellar graft loses its clarity the more serious transplantation of a penetrating graft is sure to fail. Of 270 lamellar corneal transplantations performed by Paufique, both successful and unsuccessful, transparent grafts and favorable functional results were obtained in 75 per cent. Shafer,[53] performing partial lamellar corneal transplantations on rabbits, found that no standard-sized graft persisted longer than the fifth postoperative day and that the recipient bed was epithelized at that time. He noted that standard-sized grafts, as well as over-sized grafts, showed a notch between the recipient and the donor stromal edge, presumably due to stretching of the recipient bed. The stretching and herniation of the recipient bed are not overcome by edge to edge corneal sutures. Shafer suggests that this herniation in the rabbit cornea might be avoided by a decompression procedure.

Coppez [54] is of the opinion that lamellar keratoplasty is preferable to the penetrating type because of the lessened risk. He reports on 10 cases (Amsler's technic). Keratographic studies showed that the resulting vision depended on the regularity

52. Paufique, L.: Indications for the Therapeutic Lamellar Corneal Graft, Am. J. Ophth. **33**:24 (March, pt. 2) 1950.

53. Shafer, D. M.: Experimental Lamellar Grafts of Lamellar Partial Type, Am. J. Ophth. **33**:26 (March, pt. 2) 1950.

54. Coppez, L.: Clinical and Physiopathological Study of 10 Cases of Partial Lamellar Keratoplasty, Bull. Acad. roy. de méd. de Belgique **14**:313 (July) 1949.

(curvature) of the center of the graft only. Hence he dissects the recipient bed as deep as Descemet's membrane in the central area (2 mm.). This gives the graft maximal transparency in the important, central area. He leaves the peripheral edges of the graft thick, thus helping to combat poor nutrition and vascularization. By this method, also, the graft can exert a maximal beneficial trophic effect. Hugonnier-Clayette,[55] in Paufique's clinic at Lyons reports on the therapeutic results of 41 lamellar grafts performed on 39 patients. The principal value of the operation was in the arrest of progress of the chronic or recurrent corneal disease. The frequent optical improvement was of incidental benefit. In this series of operations, 31 were successful, 2 were of doubtful outcome and 8 were failures. Conditions which responded best to this form of therapy were keratitis due to neurotropic viruses (especially herpes zoster), hypopyon ulcers with intracorneal abscesses, certain ulcerative types of keratitis, interstitial keratitis and dystrophic keratitis. Unfavorable were keratitis rosacea, tuberculous keratitis and primary corneal edema. The whole, or only parts, of the corneal surface may be replaced by a lamellar graft. It is not yet exactly known how the beneficial effects of this type of grafting come about. Evidently, some of it results from the removal of diseased tissue and its replacement with healthy tissue; but, in addition, there must be some stimulating or trophic action from the implanted foreign material.

Fine,[56] studying the clearing effect of transplanted cornea, produced permanent corneal opacities in rabbits and then performed lamellar homotransplantations and penetrating homotransplantations of identical donor material.

In series of 6 and 4 successful lamellar transplantations to the center and margins, respectively, of opacified cornea there was no clearing of the recipient cornea elsewhere than at the site of direct replacement. Of 6 animals in which partial penetrating transplants were performed with identical donor material to similarly opacified corneas, clearing of the recipient cornea around the graft was noted in 4.

The author believes that this clearing is due, at least in part, to circulatory and metabolic changes produced by the operation itself. Moreover, the failure of clearing after successful lamellar grafting suggests that the presence of the homologous tissue by itself does not fully account for the clearing.

Stansbury[57] commented on the advantages and disadvantages of the lamellar graft. Lamellar keratoplasty, being an extraocular operation, is more conservative, in that such complications as injury to the lens, prolapse of the iris, anterior synechias and secondary glaucoma do not occur. Support from the remaining, underlying cornea tends to prevent dislocation and bulging of the graft. There is greater freedom in selecting the size of the graft, and the operation is more feasible for children and uncooperative adults. However, a definite disadvantage of lamellar transplantation lies in its unsuitability to eyes with abnormalities in corneal curvature. Penetrating grafts are better suited to cases of keratoconus. Stansbury also thinks that technically lamellar grafts are more difficult to perform, in that it is not always possible to make the depth of the bed equal to that of the

55. Hugonnier-Clayette, S.: Therapeutic Lamellar Corneal Grafts, Lyons. M. Audin & Cie, 1949, p. 82.

56. Fine, M.: Clearing Effect of Transplanted Cornea on the Opacity of the Recipient Cornea, Arch. Ophth. **43**:1065 (June) 1950.

57. Stansbury, F. C.: Lamellar Corneal Transplantation: Preliminary Report, Arch. Ophth. **43**:891 (May) 1950.

thickness of the graft, and that with lamellar grafts the tissues are more likely to be subjected to trauma in handling. Many papers have appeared on the technic, indications for and complications of penetrating keratoplasty. Paton [58] gives an excellent historical review of corneal transplantation. Stansbury [59] justly criticizes some of the earlier overenthusiastic statistical reports. None of the previous reports answered questions relating to the standards of success, such as transparency of the graft or improvement in vision, complications and their effects on the final results. Nor were there any accurate statistics on indications for the procedure and percentages of successful results. He reviews the clinical records of corneal transplantations performed at the Presbyterian Hospital and postoperative follow-up studies at the Vanderbilt clinic, and reports on 165 corneal transplantations. His conclusions were as follows:

"1. There is no accord in the ophthalmologic literature concerning the results of corneal transplantation.

"2. Transparency of the graft cannot be considered adequate proof of a successful operation, because clear grafts are frequently seen without any functional improvement in the eye. Normal corneal curvature is as important as clarity of the graft in obtaining a successful optical result.

"3. Improvement in vision is the logical index of success in corneal transplantation. Inasmuch as 20/200 visual acuity is commonly accepted as the threshold for industrial blindness, it is suggested that successful results in corneal transplantation require postoperative improvement in visual acuity to better than 20/200.

"4. The visual and cosmetic results of 165 corneal transplantations, performed on 130 eyes of 110 patients, are reviewed:

"(*a*) Visual acuity was improved to better than 20/200 after 22 operations, or 13 per cent of the series. There was no significant change in visual acuity after 86 operations, or 52 per cent of the series. A loss of visual acuity followed 57 operations, or 35 per cent of the series; 20 of these operations, or 12 per cent of the series, were followed by loss of light perception.

"(*b*) Best results were obtained in cases of keratoconus; 10 of the 22 successful operations occurred in the keratoconus group.

"(*c*) Poorest results were obtained in cases with chemical burns of the cornea; none of these operations was successful.

"(*d*) The results of secondary corneal transplants were also poor; only 2 of the 35 operations in this group resulted in improved vision. Eight of these secondary operations resulted in loss of light perception.

"(*e*) Fifteen of the 22 eyes with postoperative improved visual acuity required strong minus lenses to attain this acuity. This postoperative myopia is evidence of a marked tendency of the cornea to bulge after a corneal transplant.

"(*f*) Clear grafts occurred twice as often as improvement in vision in this series of operations.

"(*g*) The average follow-up period for the entire series of operations was 37.7 months.

"5. The final visual results in the 130 eyes undergoing corneal transplantation in this series were: improved vision, 21 eyes (16 per cent); no significant change in vision, 53 eyes (41 per cent); loss of vision, 51 eyes (39 per cent), and result unknown, 5 eyes (4 per cent).

"(*a*) Results were better in the eyes with a single transplantation than in the eyes that had multiple grafts.

"6. The final visual results on the basis of the 110 patients were as follows: improved vision, 18 cases (16 per cent); no significant change in vision, 46 cases (42 per cent); loss of vision, 43 cases (39 per cent), and unknown result, 3 cases (3 per cent).

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58. Paton, T. R.: Corneal Transplantation: A Historical Review, Am. J. Ophth. **33**:3 (March, pt. 2) 1950.

59. Stansbury, F. C.: Corneal Transplantation: I. Visual and Cosmetic Results, Arch. Ophth. **42**:813 (Dec.) 1949.

"(*a*) Best results were obtained in those patients who had bilateral corneal grafts. Ten of the 20 patients in this group achieved improvements in visual acuity to better than 20/200. Three of these 10 patients obtained successful results in both eyes."

In his second paper, Stansbury [60] made a survey of 122 primary corneal transplantations. He found that, on the basis of diagnosis, visual results were best with keratoconus and poorest with chemical burns of the cornea. The results in eyes with interstitial keratitis were not significantly better than the average results for the series; this is not in accord with other reports on transplantations for this condition. In this series none of the operations performed on eyes with a primary degenerative process were successful. Success in cases of leukoma was proportional to the amount of normal corneal tissue surrounding the graft after operation. A high degree of corneal vascularization, anterior synechias or glaucoma was a distinct detriment and led to failure. Preliminary operations in both primary and secondary transplantations for correction of complications exerted little or no beneficial influence on the result in this series.

Castroviejo,[61] in discussing keratoplasty in treatment of keratoconus, brings out many important facts regarding the technic and complications in this procedure. Large grafts, from 6 to 7 mm. in diameter, are necessary. Hence square grafts of these sizes, which have a greater useful area than circular ones, are preferable. Because of the thinness of the recipient cornea and the ease of displacement of the graft, he recommends closely placed, edge to edge sutures, in addition to a continuous supporting one. He also advocates wide pupillary dilation before the operation to prevent anterior synechia. Anterior synechia is one of the most frequent complications in these cases. In order to prevent secondary glaucoma, an operation for the separation of these adhesions is mandatory, especially if they are extensive. This should be performed between the second and the third week after the original operation. Castroviejo devised a special procedure for the treatment of extensive anterior synechias.

Stansbury,[62] after describing the instruments and technic of transplantation with the circular graft, discusses the pros and cons of the circular versus the square graft. He concludes that the circular graft is technically easier to accomplish and that the results with it are visually and cosmetically better.

Barraquer,[63] Sourdille [64] and Thomas [65] all favor circular grafts. The first two authors also prefer edge to edge sutures. According to Barraquer, direct suturing with fine silk thread and extremely sharp 5 mm. needles (Grisehaber) guarantees the best results.

60. Stansbury, F. C.: Corneal Transplantation: II. Indications and Contraindications, Arch. Ophth. **43**:337 (Feb.) 1950.

61. Castroviejo, R.: Keratoplasty in Treatment of Keratoconus, Arch. Ophth. **42**:776 (Dec.) 1949.

62. Stansbury, F. C.: Circular Corneal Transplants: Surgical Technic; Instruments and Sutures; Comparison with the Use of Square Transplants, Arch. Ophth. **42**:155 (Aug.) 1949.

63. Barraquer, J. I., Jr.: Technique of Penetrating Keratoplasty, Am. J. Ophth. **33**:6 (March, pt. 2) 1950.

64. Sourdille, G. P.: The Complications of Penetrating Keratoplasty, Am. J. Ophth. **33**:17 (March, pt. 2) 1950.

65. Thomas, T.: Remarks on the Technique of Corneal Transplantation, Am. J. Ophth. **33**:66 (March, pt. 2) 1950.

In order to facilitate trephination, Lindner [66] recommends the injection of Ringer's solution into the anterior chamber during the trephining procedure, provided that the anterior chamber is visible. The injection with a certain pressure deepens the anterior chamber, and when the aqueous begins to escape through the trephine wound it will be partly replaced with Ringer's solution. Hence, additional resistance is gained to make a clearer cut through the posterior corneal surface, and time is gained for continuing the trephining without endangering the lens. Thomas [67] describes his experience with transplantation in treatment of aphakia and in cases in which the lens is displaced. He has designed special corneal spatulas to prevent loss of vitreous. The spatula is inserted into the anterior chamber through a keratome incision. The blade of the spatula may be released from its holder and stabilized by a magnet. When the displaced lens is cataractous, Thomas advises that the transplantation be performed first.

Thomas [68] also discusses the complication of corneal fistula following transplantation and the necessity for its repair. In 2 cases he was able to close the fistula either by means of cauterization or by the transplantation of mucous membrane into the fistulous tract.

In order to obtain exact apposition of the edges of the graft to the corneal bed and adequate protection for the lens and iris from the cutting instrument, Lee and Allen [69] devised an instrument consisting of a spatula which enters the anterior chamber to support the cornea and a guide for the trephine blade, both of which are attached to one handle. With it, the authors claim to be able invariably to obtain a completely excised corneal disk without recourse to additional instrumentation (scissors). They believe that this instrument possesses advantages over the Filatov prophylactic spatula.

A complete study of the effects of electrocoagulation of the sclera in regard to the reduction in ocular volume and the production of pathological changes is reported by Scheie and Jerome.[70] They found that surface electrocoagulation produces a reduction in ocular volume in enucleated eyes and eyes in living animals comparable to resections of scleral tissue 4 by 22 mm. Penetrating electrocoagulation produced a smaller reduction in volume. Reduction in ocular volume by these procedures lasted during the period of observation of two months. Electrocoagulation in the amount used in these experiments produced such extensive pathological changes in the sclera, choroid and retina as to suggest caution in its clinical use.

Lindner [71] describes his operation for shortening the eyeball (scleral resection) in cases of detached retina and reports his results in 36 eyes. In this group, 6 eyes were cured, 10 were improved, 9 were unchanged and 11 were worse. In several

66. Lindner, K. A.: Contribution to Keratoplasty, Arch. Ophth. **43**:769 (April) 1950.

67. Thomas, C. I.: Corneal Transplantation in Cases of Aphakia and Ectopia of the Lens: Selection of Cases; Technic of Operations Outlines; Report of New Instruments, Arch. Ophth. **42**:389 (Oct.) 1949.

68. Thomas, C. I.: Corneal Fistula Following Transplantation: Report of 2 Cases; Methods of Treatment, Arch. Ophth. **43**:503 (March) 1950.

69. Lee, O. S., Jr., and Allen, L.: Keratoplasty: Preliminary Report on the Development of Instruments, Am. J. Ophth. **32**:71 (Jan.) 1949.

70. Scheie, H. G., and Jerome, B.: Electrocoagulation of the Sclera: Reduction in Ocular Volume and Pathologic Changes Produced, Am. J. Ophth. **32**:60 (June, pt. 2) 1949.

71. Lindner, K.: Shortening of the Eyeball for Detached Retina, Arch. Ophth. **42**:634 (Nov.) 1949.

of the eyes which were cured the improvement in function was slow, taking almost a year. The operation is technically difficult and tiring, but the author feels that the success obtained in four cases in which the patients had only one eye and were saved from total blindness compensated for the failures.

Vail [72] advises immediate sclerotomy in the event of expulsive hemorrhage. He concludes:

> . . . (*a*) A trephine should be on every cataract instrument tray; (*b*) a sterile trephine or cataract knife should be ready on every dressing tray in the event that there is a delayed expulsive hemorrhage and (*c*) every ophthalmic surgeon and resident should be prepared for instant action in the event of a threatened expulsive hemorrhage.

Kronenberg [73] describes a new sclerotomy knife with both edges of the blade sharpened. Because of its angle, the incision is made easier, and the front end of the knife may be used as a pick.

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72. Vail, D.: Subchoroidal Expulsive Hemorrhage Occurring During Thiopental Sodium (Sodium Pentothal®) Anesthesia: Its Treatment by Sclerotomy, Arch. Ophth. **42**:562 (Nov.) 1949.

73. Kronenberg, B.: A New Sclerotomy Knife, Arch. Ophth. **42**:370 (Feb.) 1950.

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Correspondence

THE MODEL OPHTHALMOLOGIST—MODEL 488

The following parody was composed by Dr. Russell Carpenter, who teaches anatomy, histology and embryology in postgraduate course 488 in ophthalmology at Harvard. The occasion for this epic was a dinner given by the students and faculty of the postgraduate course. The editors consider that it is too good not to be shared with our readers.

THE MODEL OPHTHALMOLOGIST—MODEL 488

With music swiped from Sir Arthur Sullivan and words that would have made Mr. Gilbert pop-eyed (exophthalmic).

Especially composed for the meeting of Postgraduate Course 488 in Ophthalmology, Harvard University, Dec. 13, 1950:

I am the very model of a model ophthalmologist,
With knowledge so extensive I've no need for an apologist.
I'm quite equipped to handle any ocular adversity:
I took my basic science course at Harvard University.
I've learned ten million facts or so and I know what to do with them;
They're firmly locked within my brain and I recall a few of them.
My reputation for such intellectual fecundity
Insures that none can doubt my diagnostical profundity.
So when I start to practice on the public bulbus oculi,
I'm confident—and hopeful—that the customers will flock to me.
With knowledge so extensive, I've no need for an apologist;
I am the very model of a model ophthalmologist.

My grasp of eye anatomy leaves nothing that's correctable;
I've cut out every structure that is possibly dissectible.
Discourses on Zinn's annulus or ciliary ganglion
Are just my dish; they're subjects which no one can ever hang me on.
I know of every muscle that's at all concerned with human sight;
I call it "Müller's" when in doubt and half the time I'm bloomin' right!
There's not a cell or fiber microscopically unknown to me;
I have a name for each, including artefacts I'm prone to see.
On Schlemm's canal I speak at length; I'm sure I'll never get in a
Discussion that can quite exhaust my knowledge of the retina.
So versed am I in each detail—an ocular histologist,
I am the very model of a model ophthalmologist.

My studies in neurology are even now notorious;
I modeled every nucleus that's oculomotorius;
I followed every fiber tract; no one was more meticulous
Exploring all the stops along the median fasciculus.
Long hours I spent to culture the pestiferous bacterium;
I specialized to recognize and septicize—ad weary-um!
For optics I've a special bent, and factors aberrational
I write in sines and tangents with results oft quite sensational.
In fact I know each angle of this complicated business,
Though kappa, alpha and the rest have caused me untold dizziness.
Completely trained as any mathematical biologist,
I am the very model of a model ophthalmologist.

There's nothing basic to the eye left out of my curriculum;
It saturates my hemispheres and squeezes one colliculum!
No facts are left for me to gain in knowledge of the aqueous,
And I can promptly recognize a cataract opaqueous;
The slitted lamp reveals to me all things that may be seeable;
In short, my erudition brings a feeling most agreeable.
So though I feign, now and again, a manner lackadaisical,
This point I wish to emphasize: My sciences are basical.
Thus when, in time, I stand before St. Peter's bright and weighty gate,
And in his book 'tis writ: "He took Fair Harvard's Course Four-Eighty-Eight."
I know they'll welcome me in terms that echo my necrologist:
"He was the very model of a model ophthalmologist!"

PRINCIPLES OF OPHTHALMOLOGY

To the Editor:—The reviewer of "Principles of Ophthalmology" (ARCH. OPHTH. **44:** 758 [Nov.] 1950) considers the title misleading, as in his opinion "it is really a series of essays setting forth the author's own, and extremely original, ideas."

May I be allowed to point out that, on the contrary, there exists throughout only one idea, and one idea only, which incidentally is not even original, though it does produce original results when applied to ophthalmology. The idea is that of coordination, which, although of prime importance in all investigations, is not considered necessary in ophthalmology. It is, however, only by piecing together the varied and numerous facets produced by coordination that a comprehensive picture can be obtained of what constitutes the principles of ophthalmology.

Anatomic details, such as are cited in the review, are of themselves of little significance until they are brought into relationship with each other and with the function they have to perform. It is then possible to understand the pattern of the evolution of the eye from marsupials to the completion of mammalian perfection in man.

The importance of coordination becomes increasingly evident when the physiology of the eye is considered. Is this physiology to continue to be a special creation peculiar to ophthalmology, or does it follow the universal laws which obtain throughout nature?

Accommodation, for instance, is stated to be induced by an unstriated muscle pulling on a vascular tissue; yet a vascular tissue is never found under constant stress or an unstriated muscle that is not actuated by two nerves and does not function accordingly.

No less anomalous is the fact that, although the retina is embryologically a cerebral lobe, the conventional conception of the intraocular pressure takes no cognizance of the analogous conditions in the cranium. On the other hand, the clinical observation of the venous pressure response at the disk demonstrates not only the correlation between the two but the fact that neither accommodation nor convergence affects the intraocular pressure.

A side light on what follows from lack of coordination is presented by the use of the term "elasticity." If the term had been employed according to recognized usage, the capsule of the lens would never have been given the credit of acting as prime mover in producing increased convexity of the lens, instead of the lens fibers.

The review concludes with a caution against being too easily persuaded by argument. There can be no argument over the fact that nature exists in a state of correlation and coordination. From the instances cited above, the principles that govern ophthalmology are no exception.

THOMSON HENDERSON, M.D., Nottingham, England.

15, The Ropewalk.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

The Educational Foundation in Ophthalmic Optics.—The Educational Foundation in Ophthalmic Optics is pleased to announce the awarding of 12 scholarships of $100 each to students in opticianry attending the University of New York, Los Angeles City College and Rochester Junior College. Scholarships will be awarded on a competitive basis and according to the rules established by the advisory council of each college. The necessary promissory notes have now been prepared, making available to deserving students in any of the three colleges loans up to $500 for any one individual student, on recommendation by the dean of the college. In that way any student deserving of financial aid may be encouraged to complete his education in opticianry.

The Educational Foundation in Ophthalmic Optics is under the supervision of the American Board of Opticianry and is managed by nine trustees, representing the several branches of prescription opticianry. The $50,000 Foundation is now more than half pledged, the funds having been contributed by members of the prescription optical industry, as well as by some factories which have shown an interest in higher education for the optician, whose function it will be to interpret and fabricate prescriptions for members of the ophthalmological profession.

Postgraduate Conference in Clinical Ophthalmology.—The Stanford University School of Medicine will present a postgraduate conference in clinical ophthalmology from March 26 through March 30, 1951. Registration will be open to physicians who limit their practice to the treatment of diseases of the eye or the eye, ear, nose and throat. In order to allow free discussion by members of the conference, registration will be limited to 30 physicians. Instructors will be Dr. Edward Maumenee, Dr. Dohrmann K. Pischel, Dr. Jerome W. Bettman, Dr. Earle H. McBain, Dr. Arthur J. Jampolsky and Dr. Max Fine. Programs and further information may be obtained from Office of the Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15.

Postgraduate Convention of the Oregon Academy of Ophthalmology and Otolaryngology.—The eleventh Annual Postgraduate Convention of the Oregon Academy of Ophthalmology and Otolaryngology will be held in Portland from March 25 to March 30, inclusive. Sessions in ophthalmology are scheduled on March 26 and 27 and the morning of March 28. Included among the guest speakers are Dr. Richard Scobee, professor of ophthalmology, Washington University Medical School, St. Louis, and Dr. F. Bruce Fralick, professor of ophthalmology, University of Michigan Medical School, Ann Arbor, Mich.

Training Course in Orthoptics.—The American Orthoptic Council will present its fourth annual intensive course in orthoptics in Boston from July 5, 1951 through Aug 31, 1951. Tuition is $150. The course is designed to present the necessary basic didactic instruction for students, together with some practical instruction, in order to prepare the student to complete a course of practical training and experience offered at various orthoptic centers over the country. The Council will make an effort to see that all students enrolled in the course have places to complete their practical training after the course. Applicants must be at least 18 years of age, have had a high school education and be sponsored by an ophthal-

mologist. A few scholarships are available to students from the Delta Gamma Fraternity Project. Inquiries and applications should be addressed to the American Orthoptic Council, Dr. Richard G. Scobee, 640 South Kingshighway, St. Louis 10.

PERSONAL NEWS

The Leslie Dana Medal Award.—The Leslie Dana Medal, a national award for outstanding achievement in the prevention of blindness, was presented to Dr. William L. Benedict, Rochester, Minn., at a dinner in the Hotel Chase, St. Louis, on January 26. Dr. Benedict was selected for recognition by the St. Louis Society for the Blind, which annually awards the medal established in 1925 by Mr. Leslie Dana, of St. Louis.

The January meeting of the St. Louis Ophthalmic Society was held later in the evening. As guest speaker, Dr. Benedict spoke on "Diagnosis of Orbital Disease."

SOCIETY NEWS

National Society for the Prevention of Blindness.—Applications for research grants from the National Society for the Prevention of Blindness should be received by April 15, 1951. Funds available are for grants-in-aid for either basic laboratory or clinical research projects that will lead to increased understanding of the etiology of blinding ophthalmic disease or improve methods of diagnosis, treatment or prevention. Application forms may be obtained from Research Committee, National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

Ophthalmological Society of Egypt.—The annual meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, on Thursday and Friday, March 15 and 16, 1951. Medical practitioners, oculists or otherwise, are cordially invited.

Communications may be sent to Dar El Hekmah, 42 Kaar El Ainy St., Cairo.

Society Transactions

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Perce DeLong, M.D., Chairman
M. Luther Kauffman, M.D., Clerk
Oct. 20, 1949

Meningioma of the Tuberculum Sellae: Report of a Case. Dr. Benjamin M. Chambers (by invitation).

A patient with a tumor in the region of the optic chiasm is often seen first by the ophthalmologist because of disturbances in vision. Meningiomas in this region arise from the arachnoidal villi of the meninges covering the circle of sinuses surrounding the diaphragma sellae. The majority of meningiomas arise from the tuberculum sellae or the sulcus chiasmatis. Meningiomas are primarily fibroblastic in structure, are slow growing and do not invade the brain. Prognosis after complete removal of the tumor is good. When the tumor is located in the region of the tuberculum sellae, visual field defects may be the only significant finding. These defects may be variable, depending on the exact location of the tumor, the location of the chiasm and the size and direction of growth of the tumor.

On roentgenographic examination the sella turcica usually appears normal; there may be erosion of the anterior clinoid processes and the tuberculum sellae. The pneumoencephalogram may indicate filling defects in the cisterna chiasmatis.

In considering the differential diagnosis of meningiomas of the tuberculum sellae, one must rule out tumors of the hypophysial stalk, craniopharyngioma, suprasellar adenoma, tumors of the pituitary gland, meningiomas of the lesser and greater wings of the sphenoid bone, aneurysms of the internal carotid artery or of the anterior part of the circle of Willis and optochiasmatic arachnoiditis.

On Aug. 1, 1949 a white salesman aged 43 was admitted to the Graduate Hospital of the University of Pennsylvania with a history of progressive loss of vision in the left eye for five years and in the right eye for six months. There was no other complaint. The past history was essentially without significance. On his admission, visual acuity was 6/30, correctible to 6/15, in the right eye and was equal to light perception in the left eye. Examination of the fundus in the right eye revealed slight pallor of the disk, with slight blurring of the margins; the pallor was greater on the temporal side. The left disk was very pale, and the margins were sharp. Determination of the visual fields of the right eye on August 3 showed an irregular contraction, involving mainly the inferior nasal quadrant. The ophthalmologic, somatic and neurological examination gave otherwise normal results. The Bárány test suggested a supratentorial lesion in the midline. The results of all laboratory examinations were normal, including the Wassermann reactions of the blood and the spinal fluid. A pneumoencephalogram revealed defects in the region of the tuberculum sellae suggestive of a neoplasm.

On September 20 a meningioma of the tuberculum sellae was removed. The left optic nerve had been severely stretched by the tumor.

On the eleventh postoperative day, the visual acuity of the right eye had improved from 6/15 to 6/9, and the visual field had expanded to approach the normal size. There was no change in the left eye.

The case represents one in which the only complaints were ocular. Early recognition of the symptoms may well have resulted in preservation of sight in the now near-blind eye. This case should stress the importance of alertness and correct interpretation of findings by ophthalmologists in patients with apparently unexplained loss of vision.

DISCUSSION

DR. EDMUND B. SPAETH: I wish to repeat a few significant points. This man had been under the care of a competent ophthalmologist for five years. During those five years he became progressively blind in the right eye. He was in a sanatorium and received shock treatment for a depressive state. The patient himself said to me, "You would be depressed also, doctor, if you saw yourself going blind, and nothing was stopping it." He was admitted to the Graduate Hospital with no symptoms whatever, either of a general neurological or of a medical nature; this would lead one to suspect dysfunction of the pituitary or dysfunction in the neighborhood of the gland. He had, however, one persistent ophthalmic sign, regardless of who determined his field of vision—the technician, the resident or one of the attending physicians. All found the same consistent defect in his field of vision. He was discharged from the hospital with a diagnosis of optochiasmatic arachnoiditis.

As has been stated, he had no disturbance of the pituitary, and the electroencephalogram and roentgenograms were normal. Neither an air encephalogram taken at another hospital nor the ventriculogram at the Graduate Hospital showed any abnormality.

After his discharge from the hospital, Drs. Trueman, Yaskin and Groff reviewed these ventriculograms. One of the three expressed the belief that the area of the tuberculum sellae showed a convexity in the ventriculogram which was not normal. Because of that, a transfrontal craniotomy was done, and the tumor was found and extirpated readily.

Dr. Chamber's differential diagnosis was adequate, though brief. The two things to which he called attention were the lack of symptoms in a case of tumor of the tuberculum sellae and the striking similarity in this case to the so-called Foster Kennedy syndrome, which the patient really did not have.

DR. GLEN G. GIBSON: Dr. Chambers is correct in saying that chiasmal lesions are primarily the domain of the ophthalmologists, for these lesions are difficult to diagnose early in their course. In most cases it requires careful perimetric mapping of the fields by a physician to diagnose the lesion, as in the majority of cases the classic bitemporal hemianopsia does not appear until late in the disease. One is actually performing a neurological examination of the second cranial nerve, and the demonstration of the defect and the interpretation of the patient's responses are so complicated that this task, more than any other diagnostic procedure, is beyond the domain of the perimetry technician.

The textbook signs of suprasellar lesions require careful evaluation. For example, headache is mentioned as important, when actually it is more likely to be absent than present. The characteristic field defect of complete bitemporal hemianopsia is not frequently seen, and the lesion should be recognized before that amount of visual field is lost. The appearance of the disk, if not normal, is rather characteristic in that there may be a waxy pallor and the margins may be fuller or more blurred than in the case of the intrasellar lesions, as shown in the present case. The pallor is in sharp contrast to the dark gray of the disk in syphilitic optic nerve atrophy. Central scotoma or bitemporal scotoma is common with chiasmal lesions, and this is the mechanism that accounted for the loss of vision in this case, even though the scotoma did not show in the field illustrated.

Early recognition of meningioma of the tuberculum sellae is important because the tumor is relatively easy to remove and the return of function of the optic nerve

is sometimes amazing. It is the responsibility of the ophthalmologist to have confidence in his neurosurgical colleagues and to urge operation, as there is no other way of saving sight in cases of this type. The prognosis is much better now than it used to be; consequently, it is his responsibility to recommend the correct treatment.

Fibrin Closure in Ocular Surgery. Dr. Arno E. Town (by invitation).

The principal aim of fibrin closure is to prevent the complications incident to a leaking wound by providing even and rapid healing of the incision. Reformation of the anterior chamber begins immediately after the wound is sealed with fibrin, and in no case in which this technic of closure has been used has there been a delay in the restoration of the anterior chamber. In addition, the hemostatic property of the thrombin should lessen hemorrhage into the anterior chamber. Furthermore, the traumatism caused by the introduction of corneoscleral sutures and their postoperative removal is averted. It is believed that a perfect closure will decrease the incidence of the dreaded postoperative complications of epithelial invasion of the anterior chamber.

Sealing of ocular wounds with fibrin is secure and rapid and produces an even-healing wound. The number of leaky postoperative wounds is reduced, and the danger of hemorrhage, epithelial downgrowth, prolapse of the iris and separation of the retina may be lessened. This technic of wound closure is applicable in cataract and glaucoma surgery, in keratoplasty and in traumatic and plastic surgery.

This paper was published in full in the *American Journal of Ophthalmology* (33: 879 [June] 1950).

DISCUSSION

Dr. Carroll R. Mullen: Dr. Town's paper is inclusive of all the work that has been done to date on this interesting ophthalmologic subject. It is comparatively new to many of us. He developed the technics which he found best. He has cited the experience of other physicians who have used fibrin in the closure of surgical wounds.

All the work reported is that of clinicians, and they appear to be quite satisfied with present procedures. Unquestionably, the future holds great promise for this newer method of wound closure. After this type of treatment has been used in more cases, a detailed report on the complications will be of great interest. We should then like to hear the observations on the arrest of epithelial downgrowth, prolapse of the iris, hemorrhage and secondary glaucoma.

One of the most serious periods after cataract extraction is the first night. In older patients one sometimes encounters serious complications with the restlessness and physical activity associated with mental alterations. It would be of great importance to know whether the use of fibrin would give greater security in the prevention of postoperative complications in the first 24 hours than that now obtained with the use of corneoscleral sutures.

We should like to know whether this "physiological glue" could be used as an adjustment to the present use of sutures employed by many surgeons. In Chicago, at the 1948 meeting of the American Academy, Dr. Brown, of Cincinnati, reported his experiences with about 30 cases of unselected detachment of the retina. These cases were all of poor selection, for the experiment was not considered in cases in which there was some chance of surgical repair of the separation with accepted methods. He augmented the effect of usual diathermy treatment of detachment with the use of plasma-thrombin solution. He reported that adhesions did not occur well on a wet surface. However, results showed recovery, meaning reattachment of the retina, in about 60 per cent of cases, improvement in 30 per cent and no improvement in 10 per cent. These figures are encouraging and should leave the avenue of investigation in this field still open.

Dr. Tassman reported his own satisfactory results in keratoplasty. It may be that this type of closure may offer a barrier to growth of vessels into the transplant.

DR. I. S. TASSMAN: This is a comparatively new procedure, especially in ocular surgery. It is not long out of the experimental stage. I should like to compliment Dr. Town on his presentation. I am in a position to state that this is a new procedure which will provide adhesion of the edges of a wound. It may be considered as an adjunct to the technic of wound closure, because the wound edges will heal more readily and more quickly with the application of this so-called physiological glue.

There is no question about the gluelike property of this mixture. When 1 or 2 drops of thrombin solution is added to 1 drop of the patient's plasma, there is an immediate reaction. A mucilaginous or gluelike coagulum forms. This coagulum seals the wound and provides an immediate adhesion of wound edges. It is most useful, as Dr. Town pointed out, to aid in immediate closure after extraction of the lens; in corneal wounds, even without the use of a conjunctival flap if the wound does not gape too much; in the closure of the conjunctiva after ocular muscle surgery, particularly in children, and in keratoplasty.

Fibrin closure is particularly useful in keratoplasty. Having employed this method in a fair number of cases to date, I am convinced that the corneal grafts can be made to adhere. After cataract extraction the anterior chamber can be seen to reform within 30 minutes. Reformation of the anterior chamber can also be observed in some cases of keratoplasty before the operation is completed with the use of sutures.

There is one point in which, if I understand Dr. Town correctly, I differ slightly from him. I would not advocate elimination of the use of sutures in cataract operations because of this method. I think that corneoscleral sutures are still needed for the security that is provided during the course of the operation. At the completion of an uneventful operation, the application of the thrombin solution will seal the wound and provide more immediate closure and adhesion of the edges. Postoperative complications are also minimized. The solution can also be employed in cases of incomplete wound closure several days after cataract operation. When this results in a flat anterior chamber, the application of the plasma-thrombin solution will seal the wound and result in reformation of the chamber.

Dr. Mullen mentioned the possibility of complications. I am sure that the procedure is absolutely safe. No complications can result from its use.

With regard to epithelial downgrowth, the sealing of the wound and immediate adhesion of the edges at the time of operation will prevent this. It should be prevented in cataract operations, as well as in any other section of the cornea, traumatic or otherwise.

In cases of keratoplasty, the sutures only hold the graft in place and maintain it in position. They cannot provide adhesion of the edges of the wound. In application of the thrombin solution, however, one has a method which will provide immediate fixation and adhesion, so that healing will take place normally and union will occur more readily, quickly and surely.

(A number of slides were presented illustrating the results obtained in cases of keratoplasty with this method. These were cases of old interstitial keratitis, a case of corneal dystrophy and a case of keratoconus. In three of the cases the plasma-thrombin solution was employed in addition to the use of sutures, whereas in the others it was employed without the use of sutures.)

In cases of keratoplasty, additional factors are concerned in determining the final visual result, but the purpose here is principally to demonstrate the adhesive property of the fibrin coagulum in providing almost immediate adhesion and in maintaining that adhesion through the postoperative course. It is very possible

that in the future the procedure may be improved. In fact, I have one or two ideas in mind which may provide an improvement in the preparation and technic.

Dr. Edmund B. Spaeth: My experience in the use of thrombin and plasma has been wholly with skin grafts, and for this purpose the method is of tremendous assistance and importance. In the full thickness skin grafts, by means of this physiological glue one can eliminate entirely the use of sutures.

I was happy to hear Dr. Tassman use the word "adjunct" and to know that he does not discontinue the insertion of sutures for intraocular surgery.

It has been my experience, demonstrated by the investigation of cases, that it is not the intracapsular or the extracapsular procedure which predisposes to retinal separation with aphakia. This complication follows operation regardless of whether it is the one or the other procedure. Complicating cataract, and the very probable predisposition that patients with this condition have to uveitis, constitute the factor predisposing to retinal separation in aphakic eyes. A stormy postoperative recovery, regardless of the type of cataract, is the other predisposing factor.

Dr. James S. Shipman: I should like to say a few words concerning the discussion of the use of this material in retinal detachments.

I heard Dr. Brown's paper in Chicago, and his discussion on Dr. Tassman's paper in Philadelphia last May at the Wills Hospital conference. Some may have got the idea that Dr. Brown used fibrin alone in the cases of retinal detachment which he reported. He specifically stated that he used the fibrin in conjunction with the electrocoagulation technic, and that his purpose in using the fibrin was only to hold the retina in contact with the choroid for a sufficient time to allow the areas of coagulation to become adherent to the retina. In my opinion, this is not necessary, and this procedure adds difficulty to one which has become established and is comparatively simple; namely, the method of electrocoagulation, as devised by Gonin and later modified and developed by Safar, Lindner, Guist, Weve, Walker and many others in this country. I feel that this technic still holds the preeminent position in the treatment of retinal detachment and that it will continue to do so for many years.

I am in agreement with Dr. Tassman and Dr. Spaeth that sutures should not be entirely dispensed with in cataract surgery, and that if fibrin is used in this type of ocular surgery, it should be as an adjunct to employment of sutures.

Dr. Town is to be complimented on the work which he has done. I admire him for his faith in this material and his willingness to use it instead of sutures. To be sure, most of us did cataract extractions for many years without sutures or any material of this type, and the ultimate results were not unsatisfactory. Dr. Tassman is also to be complimented on his work with fibrin in corneal transplantation; it is my opinion that fibrin will be of most value in this type of surgery.

Dr. William E. Krewson III: I should like to ask Dr. Town a question: In cataract surgery, when you get an almost instantaneous closure of the wound with the use of fibrin, do you ever have trouble in the "toilet of the wound," that is, in the insertion of an iris spatula or the tip of an irrigator, if necessary?

Dr. Arno E. Town: First in answer to Dr. Krewson's question: I do not use the fibrin solution until after the toilet of the wound is completed and the iris is replaced. May I show four slides?

The first slide demonstrates the conjunctival incision which is advocated by Drs. Theobald and Haas, in which the incision is placed a long distance back of the limbus. The second slide illustrates what I was saying about making the keratome incision circular instead of at a tangent. In other words, the incision should be of the same curvature as that of the cornea. The next slide is a demonstration by Dr. Atkinson showing how the edges of the wound should be beveled. The lower keratome incision is along the plane of the iris. He advocates beveling the upper part of the incision. The next slide is a photograph of the

keratome which I used. It is difficult to photograph a keratome to show the curvature on the anterior surface. This keratome is just the opposite of the Berens keratome, which has a curvature on the posterior surface and which he uses for glaucoma surgery.

Influence of Drugs on Restoration of Intraocular Pressure in Normal Eyes After Paracentesis. DR. IRVING H. LEOPOLD and DR. ROBERT DAY (by invitation).

The influence of drugs was determined on the course of the intraocular pressure following paracentesis of the anterior chamber of normal rabbit eyes. The drugs tested by local instillation were pilocarpine nitrate, furtrethonium (furmethide®) iodide, methadione (mecholyl®) bromide, physostigmine sulfate, diisopropyl fluorophosphate, epinephrine, and phenylephrine hydrochloride. Tetraethylammonium chloride (etamon®), benzazoline (priscol®), dibenamine (N-N-dibenzyl-β-chloroethylamine) and diphenhydramine (benadryl®) were given intravenously. The influence of various combinations of drugs, such as diisopropyl fluorophosphate and epinephrine, methadione and epinephrine, and physostigmine and epinephrine, were studied.

The results revealed that the cholinergic drugs and the anticholinesterase agents increased the initial rise in intraocular pressure after paracentesis and prevented the secondary rise. The epinephrine-like compounds prevented or diminished the primary and secondary rises of intraocular pressure seen in the normal eye. The epinephrine-like compounds also prevented or diminished the effects on intraocular pressure of the cholinergic and anticholinesterase drugs. The sympatholytic drugs increased the primary rise in intraocular pressure after paracentesis. Antihistamine drugs diminished slightly the primary rise in intraocular pressure after paracentesis. Their influence was not so marked in this respect as the epinephrine-like compounds. Dibenamine produced an effect unlike that of other sympatholytic compounds.

These studies suggest that cholinergic and anticholinesterase agents increased the caliber of intraocular small vessels, as well as their permeability, and that the power of epinephrine compounds to produce vasoconstriction could overcome the vasodilating stimulus of paracentesis plus the effect of cholinergic and anticholinesterase drugs.

Theoretical and practical applications of these studies were suggested, and attention was directed especially to the merit of the combination of cholinergic and sympathomimetic drugs in glaucoma therapy.

The drugs employed in this study have been limited to those which are known to have an effect on ocular tension. The explanation of their actions has been limited, in the main, to their vasomotor effects. The reasons for this are twofold. First, there is no evidence that secretion of aqueous humor occurs after paracentesis and, second, it is believed that the results obtained can be adequately explained on the basis of the vasomotor effects, without the assumption of any secretory effect.

The method employed was not exact. The determination of ocular tension in rabbits with a Schiøtz tonometer is not easy. However, it was found that the results obtained were reproducible and that they agreed with observations previously reported. As an example, the effect of atropine in producing an initial rise in tension higher that that in control eyes, followed by a secondary rise, was similar to the results reported by Duke-Elder.

It is hoped that this study will stimulate further investigation of these drugs, which will lead to a better understanding of the treatment of glaucoma.

DISCUSSION

DR. I. S. TASSMAN: I should like to ask Dr. Leopold how he would suggest using tetraethylammonium chloride and benzazoline clinically in cases in which their administration might be indicated. There is no question in my mind that these

drugs have a clinical application. Benzazoline and tetraethylammonium chloride in particular are comparatively new drugs and have not had a wide use. They are known for their properties of vasodilation and might have value in treatment of hypertensive vascular disease, and perhaps also diabetes. It would be worth while to have Dr. Leopold enlarge on that point.

DR. IRVING H. LEOPOLD: Benzazoline and tetraethylammonium chloride can be used in ocular cases in which one would like to obtain considerable vasodilation. However, it should be kept in mind that these drugs greatly lower general blood pressure and that their use should be restricted, therefore, to patients who can withstand a considerable depression of systemic blood pressure. The drugs may be given parenterally or may be taken by mouth. Benzazoline (priscol®) comes in 50 mg. tablets; tetraethylammonium chloride, in approximately the same dose. One can give as much as 3 or 4 mg. per kilogram of body weight parenterally. These vasodilators may be tried in cases of occlusion of the retinal arteries of short duration and with the fundus conditions in which the retinal or uveal circulation might benefit from vasodilation. This subject is one for further study, and there have been few reports of the merits of these drugs in ocular therapeutics, except in the French literature.

Book Reviews

The Adjustment of the Blind. By Hector Chevigny and Sydell Braverman. Price, $4. Pp. 320, with no illustrations. Yale University Press, 143 Elm St., New Haven, Conn., 1950.

Here is a book which should be read by every ophthalmologist and social worker, or by anyone interested in the welfare of the blind. The senior author, Hector Chevigny, author of "My Eyes Have a Cold Nose," is himself afflicted with blindness. His collaborator, Sydell Braverman, is clinical psychologist at the Southbury Training School, in Connecticut. The book is divided into nine chapters and has a bibliography and an index.

The whole subject is considered not only as regards the adjustment and reorganization of the sightless to the modern environment, but also with respect to many of the psychological problems peculiar to those who through loss of one of their functions are separated from reality—as it is understood by those not so deprived.

The history of the care of the blind is related from the earliest days, when social ostracism was the fate of the sightless, until the present day, when recognition of the fact that the blind are still people and emotionally are no different from the rest of us, is gradually seeping through our social consciousness. For centuries an entire system of superstitions and taboos arose in connection with the eye, especially with those who were sightless. Mythology gives many instances of this, especially as the eye was considered symbolical of the sun. The works of Charles Campbell and Winifred Holt are cited as examples of what could be done in the way of the creation of organizations for training and rehabilitating the sightless.

The question rises as to what is the ideal system in which the blind may participate fully in communal life and where they may "contribute to its strength." The blind themselves do not wish to be segregated into communities. Evidently the problem of all handicapped persons will have to be considered from the standpoint of a governmental enterprise, rather than at the existing local or state levels.

The ophthalmologist will do well to read the chapter pertaining to the handling of patients approaching blindness. How forthright should he be? It is human to shy away from the task of bringing bad or hopeless and shocking prognoses. Most ophthalmologists try to break the news gradually or endeavor to soften the blow so as not to take away all hope. In doing this they are often placed in the position of withholding what they know to be the bald truth. Does such preparation avoid or diminish the eventual shock?

According to the author, "Eye patients then, far more than any others, should be given preparation for what may happen to them. The ophthalmologist should be one of the best psychologists in the medical profession, not one of the worst. There seems little alternative but to pose for himself the same rule his code dictates, where the knife is concerned. The knife, when occasion dictates, must be grasped; truth likewise must not be withheld when it is known. Only by the rule of telling the truth can the eye surgeon make the best guess for the safety of his patient."

At last, the problems of the sightless are being considered in an intelligent and rational way.

Essentials of Ophthalmology. By Roland I. Pritikin, M.D. Price, $7.50. Pp. 561, with 215 illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia.

The author has used an interestingly new and logical approach in his condensed version of ophthalmology for the general practitioner and the medical student. Especially commendable is his use of new illustrations, since many of them are definite improvements over ones usually employed.

As is to be expected in the first edition of a book which is so comprehensive and so condensed, there are some errors, some ambiguous statements and some lack of coverage of recent literature. For example, while excellent in many respects, the section on physiology of the eye is lacking in detail on present concepts of vascular physiology; and the presently accepted views on the mechanism of drug actions are not covered. However, the more serious errors are made in the section on inflammatory diseases of the eyes. For example, under blepharitis two of the commonest types of the disease (staphylococcic and seborrheic) are not mentioned. Only the least common agents (Hemophilus duplex and parasites) are given among many traditionally listed, but relatively insignificant, contributory causes. Under acute catarrhal conjunctivitis, the ambiguous statement, "The organisms most commonly found in this condition are: (1) Morax-Axenfeld diplobacillus (or H. duplex), (2) bacillus xerosis, (3) staphylococcus, (4) pneumococcus, (5) streptococcus, (6) micrococcus catarrhalis," is erroneous, because repeated observations in the Midwest indicate that the common causes of acute catarrhal conjunctivitis in order of frequency are (1) Pneumococcus, (2) Streptococcus viridans, (3) Staphylococcus, (4) Hemophilus influenzae, etc. The Corynebacterium xerose (Bacillus xerosis) should not be listed in this manner, as it implies that this normal inhabitant of the conjunctiva is the cause of conjunctivitis. The Morax-Axenfeld diplobacillus (H. duplex) is a rare cause of conjunctivitis, especially in the Midwest and in the northern part of the United States. The organism, however, frequently is the cause of blepharitis and chronic blepharoconjunctivitis in the hot and dusty parts of this country. Micrococcus catarrhalis (Neisseria catarrhalis) is a rare cause of conjunctivitis. Again, under chronic catarrhal conjunctivitis the most frequent cause of the disease, Staphylococcus, is not mentioned.

The author introduces the term "swimming pool conjunctivitis" for bacterial lesions acquired while swimming. This is unfortunate and confusing, since "swimming pool conjunctivitis" has been used widely to mean the adult form of inclusion blennorrhea. Even this should be condemned, since it is possible to make a specific positive diagnosis, adult inclusion blennorrhea.

Treatment of the infectious diseases is oversimplified or erroneous in many instances, as an antibiotic is recommended which is ineffective —for example, penicillin for vernal conjunctivitis, trachoma, leptotrichosis of the conjunctiva (Parinaud's conjunctivitis) and several gram-negative bacillus infections. It is unfortunate that the author should advocate the indiscriminate use of these drugs, many of which may produce added difficulties for the patient by sensitivity reactions.

The chapter on medicolegal ophthalmology is a welcome addition to a book of this type, and the numerous tables are valuable for the student. It is to be hoped, therefore, that the author can revise the material soon.

Fundamentals of Optics. Second Edition. By Francis A. Jenkins and Harvey E. White. Price, $7. Pp. 647. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18, 1950.

The first edition of this text represented an advanced undergraduate course in optics. It was assumed that the student had completed a thorough course in elementary physics and was familiar with the methods of calculus. It was considered one of the best standard texts for advanced optics.

In this second edition the authors have added 10 chapters on geometric optics, which serve the purpose of an introduction to the rest of the book for the elementary student. These are concise and well illustrated. A number of problems are given at the end of each chapter which give the book value as a text for students.

The second part of the book deals with physical optics, and the last section, with quantum optics. Both of these sections are beyond the horizon of the ophthalmologist, save for those who are advanced students of the subject and have mathematical facility.

The Cerebral Cortex of Man: A Clinical Study of Localization of Function. By Wilder Penfield and Theodore Rasmussen. Price, $6.50. Pp. 248, with illustrations. The Macmillan Company, 60 5th Ave., New York 11, 1950.

In this monograph the senior author reports his observations, made over many years, on the effects of stimulation and ablation of portions of the human brain. The source material was approximately 400 craniotomies. While of particular interest to the neurosurgeon, neurologist, psychiatrist and neurophysiologist, there is so much reference to the eye that the ophthalmologist will find it of considerable interest and profit. The following is a partial résumé of the authors' observations on the ocular motor and ocular sensory system.

Unlike the strict lateralization of cerebral functions that applies to the extremities, the eye representation in one hemisphere is often bilateral. Thus, stimulation of selected points in one postcentral gyrus gives rise to ocular sensations, "queer feelings," about as often referred to both eyes as to one eye; similarly, stimulation of one precentral gyrus produces bilateral brow movements and eyelid movements as often as it does unilateral movements.

While there was considerable individual variation, the loci which elicited deviation of the eyes to the opposite side were scattered either about the anterior lip of the rolandic fissure or anterior to it, in the precentral gyrus; in either case they were situated above the area representing face and below the area representing thumb. In comparison with that in animals, the representation in man appears to have been displaced backward.

The regions of the postcentral gyrus which produced sensations referred to the eye were similarly to be found between the thumb and the face area and were often accompanied with movements of the eye, so that the authors consider corresponding parts of the precentral and postcentral gyri as a sensorimotor unit. Eyelid movements, either opening or closing or both, were to be elicited by stimulation of the same general areas as for eye movements but tended to be closer to the rolandic fissure.

Stimulation of the occipital cortex elicited elementary sensations of light, color and shapes, and it made little difference whether the region stimulated was Brodmann's area 17, 18 or 19. (Almost all the observations were necessarily limited, however, to the lateral aspect of the brain.) It is somewhat surprising to learn that the phosphene was referred to the bilateral or ipsilateral field about as often as to the contralateral field. Not until portions of the temporal cortex were reached did integrated visual hallucinations occur.

A Syllabus of Laboratory Examinations in Clinical Diagnosis. Thomas Hale Ham, M.D. Price, $5. Pp. 496. Harvard University Press, Cambridge 38, Mass.

This is a compilation of the various diagnostic procedures through which patients must be put in a diagnostic clinic. The book is of interest to the ophthalmologist only in keeping him up to date with what procedures are advocated by the well known group of physicians and surgeons who have contributed to this syllabus. This reviewer's only criticism is that it is not set in type, but has been done by one of the modern photographic processes, which makes reading very difficult.

Slit Lamp Microscopy of the Posterior Segment. By Karl Hruby, M.D., Assistent an der 2. Universitäts-Augenklinik Wein. First Edition. Price, $6.80. Pp. 164, with 20 illustrations in text and supplement of 32 illustrations in color. Urban & Schwarzenberg, Frankgasse, Vienna 4, 1950.

This is a German text describing Hruby's methods of examination of the posterior segment with contact glass and slit lamp.

The book is well organized and well illustrated and, to those who employ his method, will be most useful.

The color plates illustrative of vitreous detachments and retinal tears and disinsertions are particularly illuminating.

Manuel d'ophtalmologie. By P. Bailliart and A. Magitat. Pp. 1166. Gaston Doin et Cie, 8 Place de l'Odion, Paris, 6e; Masson et Cie, 120 Boulevard Saint-Germain, Paris, 6e, 1950.

This excellent new text in French comes from the pens of two ophthalmologists well known in this country for their work on ophthalmodynamometry and physiology of the eye, respectively. The text, of 1,166 pages, follows the usual anatomic division of ocular diseases. Part 1 contains chapters on the general examination of the patient, ocular pain, special technics used by ophthalmologists, including a short description of gonioscopy, and a short chapter on general laboratory studies. In view of the condensation necessary in most of the book, it seems to the reviewer that this chapter could have been omitted to save space.

Part 2 deals with the diseases of the eye and orbit; part 3 covers the field of surgery, and part 4 is concerned with refractive errors and their correction.

The illustrations are excellent, and the text is easy to read for any one with an elementary knowledge of French.

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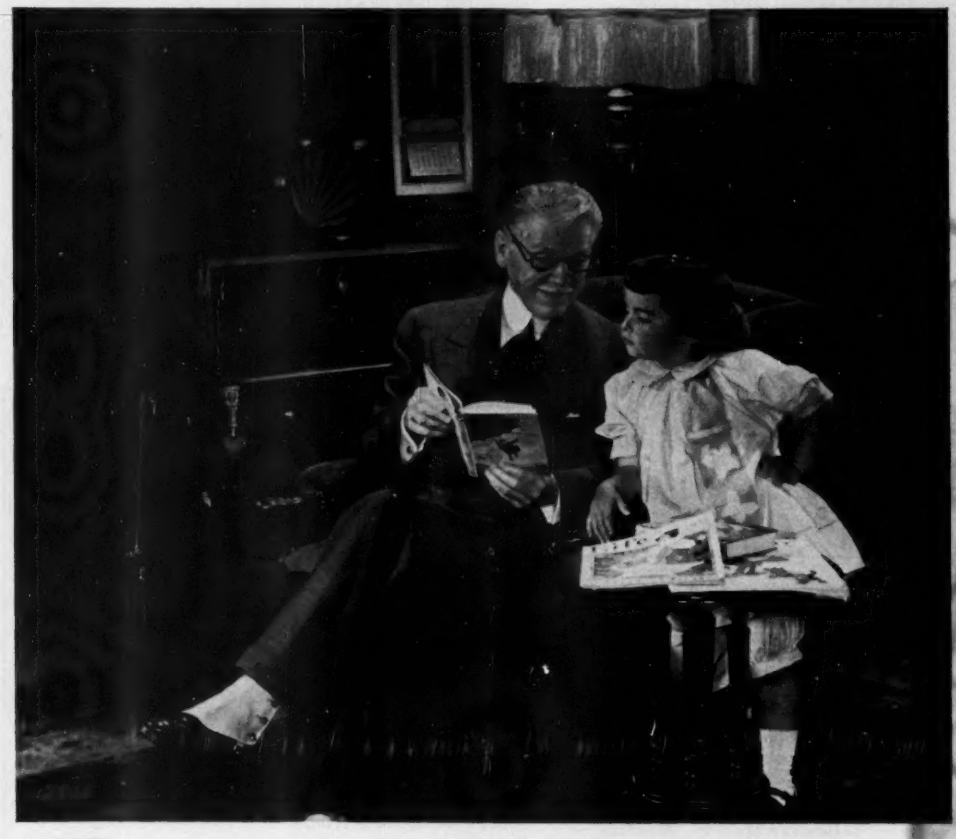

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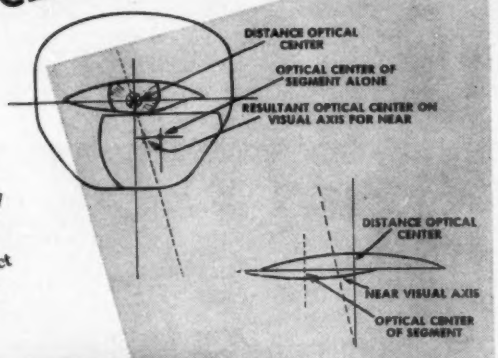
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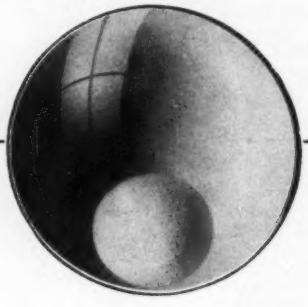

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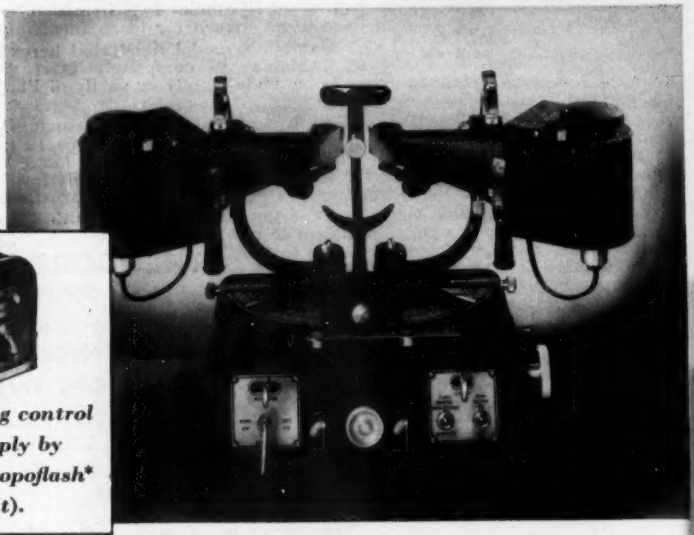

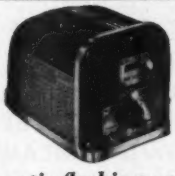

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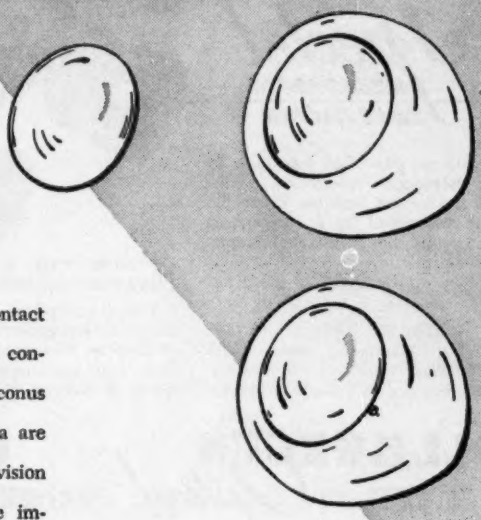

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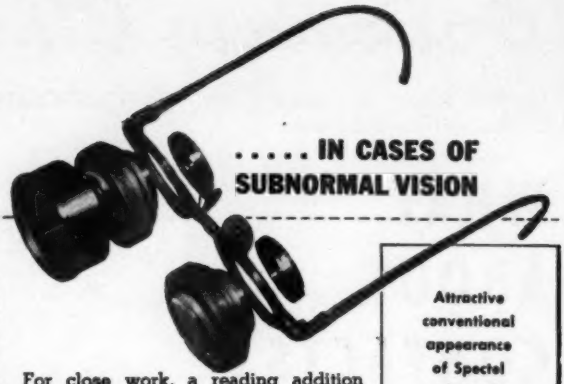

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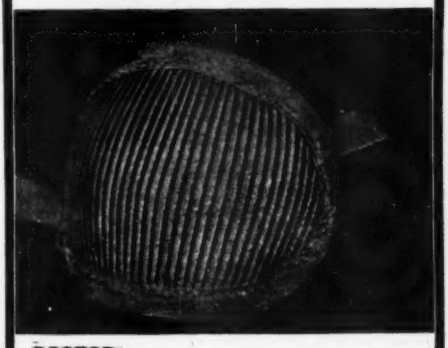

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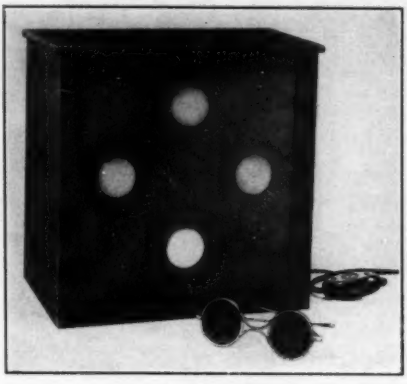

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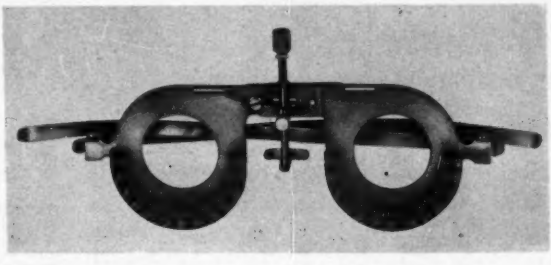

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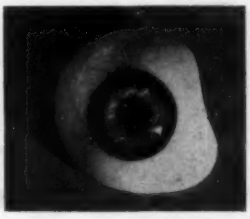

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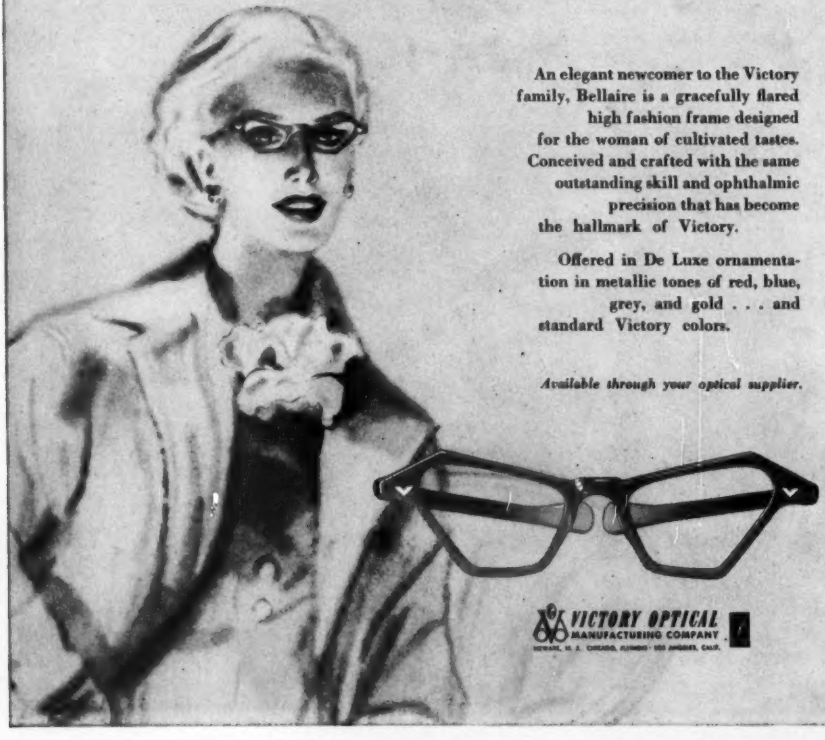

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